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INDEX 'ADISCTI, ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, ANTE, AQUALINE,
AQUASCI, BIOENG, BIOSIS, BIOTECHABS, BIOTECHDS, BIOTECHNO, CABA, CAPLUS,
CEABA-VTB, CIN, CONFSCI, CROPB, CROPU, DDFB, DDFU, DGENE, DISSABS, DRUGB,
DRUGMONOG2, DRUGU, EMBAL, EMBASE, ...' ENTERED AT 21:50:50 ON 16 JUN 2006
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L1

D RANK

FILE 'USPATFULL, BIOTECHDS, WPIDS, LIFESCI, ESBIOBASE, BIOTECHNO, CAPLUS,
IFIPAT, USPAT2' ENTERED AT 21:55:37 ON 16 JUN 2006

L2 7298 SEA LYSIN?(S)(PRODUC? OR SYNTH?)(S) BACTER?

L3 11640 SEA LYSI?(S)(PRODUC? OR SYNTHE?)(S)(COLI? OR ESCHERI? OR
BREVIB? OR CORY? OR GLUTAMICU? OR ACTINO? OR ARTHRO?)

L4 31 SEA L3(S)(PIMEL?)

L5 22 DUP REM L4 (9 DUPLICATES REMOVED)
D TI L5 1-22
D IBIB ABS L5 6-8, 10, 13, 15-21
D KWIC L5 6-8, 10, 13, 15-21

L6 424 SEA L3(S)(PIMEL? OR DIAMINOPIMEL?)

L7 221 SEA L6(S)(ANAL? OR INHIBI?)

L8 161 DUP REM L7 (60 DUPLICATES REMOVED)

L9 113 SEA L8(S)(GENE? OR DNA? OR POLYNUCL? OR MRNA? OR CDNA?)

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NEWS 7 FEB 27 New STN AnaVist pricing effective March 1, 2006
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NEWS 17 MAY 11 KOREAPAT updates resume
NEWS 18 MAY 19 Derwent World Patents Index to be reloaded and enhanced
NEWS 19 MAY 30 IPC 8 Rolled-up Core codes added to CA/CAplus and USPAT FULL/USPAT2
NEWS 20 MAY 30 The F-Term thesaurus is now available in CA/CAplus
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=> index bioscience medicine
FILE 'DRUGMONOG' ACCESS NOT AUTHORIZED
COST IN U.S. DOLLARS
FULL ESTIMATED COST

| SINCE FILE ENTRY | TOTAL SESSION |
|------------------|---------------|
| 0.21 | 0.21 |

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71 FILES IN THE FILE LIST IN STNINDEX

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=> s lysin?(s) (produc? or synth?) (s)bacter?

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10746 FILE DGENE

23 FILES SEARCHED...

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34 FILES SEARCHED...

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48 FILES SEARCHED...

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7 FILE PHIN

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56 FILES HAVE ONE OR MORE ANSWERS, 71 FILES SEARCHED IN STNINDEX

L1 QUE LYSIN? (S) (PRODUC? OR SYNTH?) (S) BACTER?

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| F50 | 3 | IPA |
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| F56 | 1 | NAPRALERT |

=> file f2-f10, f12,f14
COST IN U.S. DOLLARS

FULL ESTIMATED COST

| SINCE FILE ENTRY | TOTAL SESSION |
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=> s lysin?(s) (produc? or synth?)(s)bacter?
3 FILES SEARCHED...
L2 7298 LYSIN?(S) (PRODUC? OR SYNTH?)(S) BACTER?

=> s lysi?(s) (produc? or synthe?)(s) (coli? or escheri? or brevib? or cory? or glutamicu? or actino? or arthro?)

3 FILES SEARCHED...
8 FILES SEARCHED...
L3 11640 LYSI?(S) (PRODUC? OR SYNTHE?)(S) (COLI? OR ESCHERI? OR BREVIB? OR CORY? OR GLUTAMICU? OR ACTINO? OR ARTHRO?)

=> s 13(s) (pimel?)
L4 31 L3(S) (PIMEL?)

=> dup rem 14
PROCESSING COMPLETED FOR L4
L5 22 DUP REM L4 (9 DUPLICATES REMOVED)

=> d ti 15 1-22

L5 ANSWER 1 OF 22 USPATFULL on STN
TI Nucleotide sequence of the haemophilus influenzae Rd genome, fragments thereof, and uses thereof

L5 ANSWER 2 OF 22 USPATFULL on STN
TI Corynebacterium glutamicum genes encoding phosphoenolpyruvate: sugar phosphotransferase system proteins

L5 ANSWER 3 OF 22 USPATFULL on STN DUPLICATE 1
TI NUCLEOTIDE SEQUENCE OF THE HAEMOPHILUS INFLUENZAE RD GENOME, FRAGMENTS THEREOF, AND USES THEREOF

L5 ANSWER 4 OF 22 USPATFULL on STN DUPLICATE 2
TI Process for the production of L-lysine using coryneform bacteria

L5 ANSWER 5 OF 22 USPATFULL on STN DUPLICATE 3
TI Process for the production of L-lysine using coryneform bacteria

L5 ANSWER 6 OF 22 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
TI Production of L-lysine, comprises fermentation of L-lysine producing coryneform bacteria resistant to diaminopimelic acid analog, enrichment of L-lysine in medium, isolation of L-lysine or its feedstuffs additive from fermentation broth;
involving culture medium optimization and fermentation

L5 ANSWER 7 OF 22 USPATFULL on STN
TI tdcBC/pckA gene-inactivated microorganism and method of producing L-threonine using the same

L5 ANSWER 8 OF 22 USPATFULL on STN
TI Overcoming DAPA aminotransferase bottlenecks in biotin vitamers biosynthesis

L5 ANSWER 9 OF 22 USPATFULL on STN
TI Nucleotide sequence of the haemophilus influenza Rd genome, fragments thereof, and uses thereof

L5 ANSWER 10 OF 22 USPATFULL on STN
TI Corynebacterium glutamicum genes encoding metabolic pathway proteins

L5 ANSWER 11 OF 22 USPATFULL on STN
TI Nucleotide sequence of the Haemophilus influenzae Rd genome, fragments thereof, and uses thereof

L5 ANSWER 12 OF 22 USPATFULL on STN
TI Nucleotide sequence of the Haemophilus influenzae Rd genome, fragments thereof, and uses thereof

L5 ANSWER 13 OF 22 USPATFULL on STN DUPLICATE 5
TI OVERCOMING DAPA AMINOTRANSFERASE BOTTLENECKS IN BIOTIN VITAMERS BIOSYNTHESIS

L5 ANSWER 14 OF 22 LIFESCI COPYRIGHT 2006 CSA on STN DUPLICATE 6
TI Identification of the Human Mitochondrial Oxodicarboxylate Carrier BACTERIAL EXPRESSION, RECONSTITUTION, FUNCTIONAL CHARACTERIZATION, TISSUE DISTRIBUTION, AND CHROMOSOMAL LOCATION

L5 ANSWER 15 OF 22 Elsevier BIOBASE COPYRIGHT 2006 Elsevier Science B.V.
on STN
DUPLICATE

TI The three-dimensional structure of the ternary complex of Corynebacterium
glutamicum diaminopimelate dehydrogenase-NADPH-L-2-amino-6-methylene-
pimelate

L5 ANSWER 16 OF 22 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
TI Recombinant DNA autonomously replicable in coryneform bacteria -
used to produce L-lysine, codes for e.g.
aspartokinase, di hydropicolinate reductase and synthase and di amino-
pimelate decarboxylase.

L5 ANSWER 17 OF 22 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
TI Vector containing di amino pimelate decarboxylase and di amino
pimelate dehydrogenase genes - used for lysine
production by overexpression in coryneform bacteria.

L5 ANSWER 18 OF 22 USPATFULL on STN
TI Cloning of the bioA, bioD, bioF, bioC and BioH genes of bacillus
sphaericus, vectors and transformed cells

L5 ANSWER 19 OF 22 USPATFULL on STN
TI Coryneform bacteria carrying recombinant plasmids and their use in the
fermentative production of L-lysine

L5 ANSWER 20 OF 22 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
TI L-Lysine production by fermentation - using Corynebacterium microorganism
containing recombinant plasmid with fragment coding for protein which
decarbonises di amino-pimelic acid.

L5 ANSWER 21 OF 22 BIOTECHNO COPYRIGHT 2006 Elsevier Science B.V. on STN
TI Purification and characterization of succinyl-CoA: Tetrahydrodipicolinate
N-succinyltransferase from Escherichia coli

L5 ANSWER 22 OF 22 LIFESCI COPYRIGHT 2006 CSA on STN DUPLICATE 8
TI Colicin M is an inhibitor of murein biosynthesis.

=> d ibib abs 15 6-8, 10, 13, 15-21

L5 ANSWER 6 OF 22 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
DUPLICATE 4

ACCESSION NUMBER: 2004-09352 BIOTECHDS
TITLE: Production of L-lysine, comprises fermentation of L-lysine
producing coryneform bacteria resistant to diaminopimelic
acid analog, enrichment of L-lysine in medium, isolation of
L-lysine or its feedstuffs additive from fermentation broth;
involving culture medium optimization and fermentation

AUTHOR: BATHE B; HANS S; PFEFFERLE W
PATENT ASSIGNEE: DEGUSSA AG
PATENT INFO: WO 2004013341 12 Feb 2004
APPLICATION INFO: WO 2003-EP7474 10 Jul 2003
PRIORITY INFO: DE 2002-1035028 31 Jul 2002; DE 2002-1035028 31 Jul 2002
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2004-191378 [18]
AN 2004-09352 BIOTECHDS
AB DERWENT ABSTRACT:
NOVELTY - Production (M1) of L-lysine, involves
fermentation of the L-lysine producing
coryneform bacteria that are at least resistant to diaminopimelic
acid analog, in particular 4-hydroxydiaminopimelic acid, enrichment of
the L-lysine in the medium or in the bacterial cells, and
optionally, isolation of the L-lysine or L-lysine

-containing feedstuffs additive from the fermentation broth.

DETAILED DESCRIPTION - Production (M1) of L-lysine , involves fermentation of the L-lysine producing coryneform bacteria that are at least resistant to diaminopimelic acid analog, in particular 4-hydroxydiaminopimelic acid, enrichment of the L-lysine in the medium or in the bacterial cells, and optionally, isolation of the L-lysine or L-lysine -containing feedstuffs additive from the fermentation broth, such that at least 0-100% of the constituents from the fermentation broth and/or from the biomass are present. INDEPENDENT CLAIMS are also included for the following: (1) mutants of coryneform bacteria producing L-lysine and that are resistant to one or more of the diaminopimelic acid analogs chosen from 4-fluorodiamino-pimelic acid, 4-hydroxydiaminopimelic acid, 4-oxo-diaminopimelic acid or 2,4,6-triaminopimelic acid; and (2) feedstuffs additives based on fermentation broth, comprising L-lysine produced by (M1) and biomass and/or constituents from the fermentation broth formed during the fermentation of the L-lysine-producing microorganisms in an amount of 0-5% or 90-100%.

BIOTECHNOLOGY - Preferred Method: In (M1), the bacteria used comprises genes of the biosynthesis pathway of L-lysine are enhanced. The bacteria are used in which the metabolic pathways that reduce the formation of L-lysine are at least partially switched off. The production of L-lysine coryneform microorganisms are fermented in which at the same time one or more of the genes chosen from following group is/are enhanced, in particular overexpressed: the gene lysC coding for a feedback-resistant aspartate kinase, the gene dapA coding for dihydridipicolinate synthase, the gene gap coding for glyceraldehyde-3-phosphate dehydrogenase, the gene pyc coding for pyruvate carboxylase, the gene zwf coding for glucose-6-phosphate dehydrogenase, simultaneously the gene lysE coding for the lysine export protein, the gene zwal coding for the Zwal protein, the gene lysA coding for diaminopimelic acid decarboxylase, the gene sigC coding for the sigma factor C, the gene tpi coding for triose phosphate isomerase, or the gene pgk coding for 3-phosphoglycerate kinase. The production of L-lysine coryneform microorganisms are fermented in which at the same time one or more of the genes chosen from the following group is/are attenuated: the pck gene coding for phosphoenol pyruvate carboxykinase, the pgi gene coding for glucose-6-phosphate-isomerase, the gene deaD coding for DNA helicase, the gene citE coding for citrate lysase, the gene menE coding for O-succinylbenzoic acid CoA-ligase, the gene mikE17 coding for the transcription regulator MikE17, the gene poxB coding for pyruvate oxidase, or the gene zwa2 coding for the Zwa2 protein. The mutants of coryneform bacteria are used that produce L-lysine and that are resistant to one or more of the diaminopimelic acid analogs.

USE - (M1) is useful for producing L-lysine, where the microorganisms of the species *Corynebacterium glutamicum* are used that are resistant to 4-hydroxydiaminopimelic acid (claimed).

ADVANTAGE - (M1) is an improved process for the fermentative production of L-lysine.

EXAMPLE - To produce L-lysine, the following test was done. The *Corynebacterium glutamicum* strain DSM 15662Hdapr obtained was cultured in a nutrient medium suitable for the production of lysine and the lysine content in the culture supernatant was determined. The strains were first of all incubated on agar plates for 24 hours at 33 degrees C. Using this agar plate culture a preculture was inoculated (10 ml of medium in a 100 ml Erlenmeyer flask). The medium MM was used as medium for the preculture. The preculture was incubated for 24 hours at 33 degrees C at 240 rpm on a vibrator. Using this preculture a main culture was inoculated such that the initial optical density (OD-660 nm) of the main culture was 0.1 OD. The medium MM was also used for the main culture.

Culturing was carried out in a 10 ml volume in a 100 ml Erlenmeyer flask equipped with baffles. The culturing was carried out at 33 degrees C and 80% atmospheric humidity. After 72 hour, the OD was determined at a measurement wavelength of 660 nm with a Biomek 1000 instrument. The amount of lysine formed was determined by ion exchange chromatography and post-column derivatisation with ninhydrin detection, using an amino acid analyzer from Eppendorf-BioTronik. The result showed that high levels of L-lysine was produced by DSM 15662Hdapr (18.9 g/l) than the control DSM 15662 (16.2 g/l). (25 pages)

L5 ANSWER 7 OF 22 USPATFULL on STN

ACCESSION NUMBER: 2004:307160 USPATFULL
 TITLE: tdcBC/pckA gene-inactivated microorganism and method of producing L-threonine using the same
 INVENTOR(S): Park, Young Hoon, Gyeonggi-do, KOREA, REPUBLIC OF
 Lee, Byoung Choon, Seoul, KOREA, REPUBLIC OF
 Kim, Dae Cheol, Gyeonggi-do, KOREA, REPUBLIC OF
 Lee, Jin Ho, Gyeonggi-do, KOREA, REPUBLIC OF
 Cho, Jae Yong, Gyeonggi-do, KOREA, REPUBLIC OF

| | NUMBER | KIND | DATE |
|---------------------|----------------|------|---------------|
| PATENT INFORMATION: | US 2004241831 | A1 | 20041202 |
| APPLICATION INFO.: | US 2004-817044 | A1 | 20040402 (10) |

| | NUMBER | DATE |
|-----------------------|--|----------|
| PRIORITY INFORMATION: | KR 2003-21458 | 20030404 |
| DOCUMENT TYPE: | Utility | |
| FILE SEGMENT: | APPLICATION | |
| LEGAL REPRESENTATIVE: | BAKER & BOTTS, 30 ROCKEFELLER PLAZA, NEW YORK, NY, 10112 | |
| NUMBER OF CLAIMS: | 24 | |
| EXEMPLARY CLAIM: | 1 | |
| NUMBER OF DRAWINGS: | 3 Drawing Page(s) | |
| LINE COUNT: | 651 | |

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention provide a microorganism comprising an inactivated chromosomal tdcBC gene and an inactivated chromosomal pckA gene, which has remarkably improved productivity of L-threonine. Also, the present invention provides a method of producing L-threonine using the microorganism. The microorganism is prepared by incorporating by a recombination technique an antibiotic resistance gene into a pckA gene on the chromosome of a bacterial strain containing an L-threonine degradation-associated operon gene, tdcBC, which is inactivated. The microorganism has the effect of preventing degradation and intracellular influx of L-threonine due to the inactivation of the tdcBC operon gene, and includes more activated pathways for L-threonine biosynthesis. Therefore, the microorganism is useful for mass production of L-threonine because of being capable of producing L-threonine in high levels and high yields even in the presence of high concentrations of glucose.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 8 OF 22 USPATFULL on STN

ACCESSION NUMBER: 2004:190227 USPATFULL
 TITLE: Overcoming DAPA aminotransferase bottlenecks in biotin vitamers biosynthesis
 INVENTOR(S): Van Arsdell, Scott W., Lexington, MA, UNITED STATES
 Yocum, R. Rogers, Lexington, MA, UNITED STATES
 Perkins, John B., Reading, MA, UNITED STATES
 Pero, Janice G., Lexington, MA, UNITED STATES
 PATENT ASSIGNEE(S): ROCHE VITAMINS, INC. (U.S. corporation)

| | NUMBER | KIND | DATE |
|-----------------------|---|------|---------------|
| PATENT INFORMATION: | US 2004146997 | A1 | 20040729 |
| APPLICATION INFO.: | US 2004-754982 | A1 | 20040109 (10) |
| RELATED APPLN. INFO.: | Continuation of Ser. No. US 1997-914332, filed on 14 Jul 1997, GRANTED, Pat. No. US 6737256 | | |
| DOCUMENT TYPE: | Utility | | |
| FILE SEGMENT: | APPLICATION | | |
| LEGAL REPRESENTATIVE: | Stephen M. Haracz, BRYAN CAVE LLP, 1290 Avenue of the Americas, New York, NY, 10104-3300 | | |
| NUMBER OF CLAIMS: | 31 | | |
| EXEMPLARY CLAIM: | 1 | | |
| NUMBER OF DRAWINGS: | 4 Drawing Page(s) | | |
| LINE COUNT: | 798 | | |

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A method is disclosed for the increased production of biotin and the biotin precursor dethiobiotin using a bacterium that produces a lysine-utilizing DAPA aminotransferase. The method involves the use of a bacterium that is either grown in the presence of lysine or deregulated for lysine biosynthesis.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 10 OF 22 USPATFULL on STN
 ACCESSION NUMBER: 2003:71519 USPATFULL
 TITLE: Corynebacterium glutamicum genes encoding metabolic pathway proteins
 INVENTOR(S): Pompejus, Markus, Freinsheim, GERMANY, FEDERAL REPUBLIC OF
 Kroger, Burkhard, Limburgerhof, GERMANY, FEDERAL REPUBLIC OF
 Schroder, Hartwig, Nussloch, GERMANY, FEDERAL REPUBLIC OF
 Zelder, Oskar, Speyer, GERMANY, FEDERAL REPUBLIC OF
 Haberhauer, Gregor, Limburgerhof, GERMANY, FEDERAL REPUBLIC OF
 Kim, Jun-Won, Seoul, KOREA, REPUBLIC OF
 Lee, Heung-Shick, Seoul, KOREA, REPUBLIC OF
 Hwang, Byung-Joon, Seoul, KOREA, REPUBLIC OF

| | NUMBER | KIND | DATE |
|-----------------------|---|------|--------------|
| PATENT INFORMATION: | US 2003049804 | A1 | 20030313 |
| APPLICATION INFO.: | US 2000-746660 | A1 | 20001222 (9) |
| RELATED APPLN. INFO.: | Continuation-in-part of Ser. No. US 2000-606740, filed on 23 Jun 2000, PENDING Continuation-in-part of Ser. No. US 2000-603124, filed on 23 Jun 2000, PENDING | | |

| | NUMBER | DATE |
|-----------------------|--|---------------|
| PRIORITY INFORMATION: | DE 1999-19931420 | 19990708 |
| | US 1999-141031P | 19990625 (60) |
| | US 1999-142101P | 19990702 (60) |
| | US 1999-148613P | 19990812 (60) |
| | US 2000-187970P | 20000309 (60) |
| DOCUMENT TYPE: | Utility | |
| FILE SEGMENT: | APPLICATION | |
| LEGAL REPRESENTATIVE: | LAHIVE & COCKFIELD, 28 STATE STREET, BOSTON, MA, 02109 | |
| NUMBER OF CLAIMS: | 47 | |
| EXEMPLARY CLAIM: | 1 | |
| LINE COUNT: | 15004 | |

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Isolated nucleic acid molecules, designated MP nucleic acid molecules, which encode novel MP proteins from Corynebacterium glutamicum are described. The invention also provides antisense nucleic acid molecules,

recombinant expression vectors containing MP nucleic acid molecules, and host cells into which the expression vectors have been introduced. The invention still further provides isolated MP proteins, mutated MP proteins, fusion proteins, antigenic peptides and methods for the improvement of production of a desired compound from *C. glutamicum* based on genetic engineering of MP genes in this organism.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 13 OF 22 USPATFULL on STN DUPLICATE 5
ACCESSION NUMBER: 2002:185643 USPATFULL
TITLE: OVERCOMING DAPA AMINOTRANSFERASE BOTTLENECKS IN BIOTIN VITAMERS BIOSYNTHESIS
INVENTOR(S): VAN ARSDELL, SCOTT W., LEXINGTON, MA, UNITED STATES
YOCUM, R. ROGERS, LEXINGTON, MA, UNITED STATES
PERKINS, JOHN B., READING, MA, UNITED STATES
PERO, JANICE G., LEXINGTON, MA, UNITED STATES

| | NUMBER | KIND | DATE |
|-----------------------|--|------|--------------|
| PATENT INFORMATION: | US 2002098556 | A1 | 20020725 |
| | US 6737256 | B2 | 20040518 |
| APPLICATION INFO.: | US 1997-914332 | A1 | 19970714 (8) |
| DOCUMENT TYPE: | Utility | | |
| FILE SEGMENT: | APPLICATION | | |
| LEGAL REPRESENTATIVE: | MARK E. WADDELL, ESQ., BRYAN CAVE LLP, 245 PARK AVENUE, NEW YORK, NY, 10167-0034 | | |
| NUMBER OF CLAIMS: | 31 | | |
| EXEMPLARY CLAIM: | 1 | | |
| NUMBER OF DRAWINGS: | 4 Drawing Page(s) | | |
| LINE COUNT: | 951 | | |

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A method is disclosed for the increased production of biotin and the biotin precursor dethiobiotin using a bacterium that produces a lysine-utilizing DAPA aminotransferase. This method involves the use of a bacterium that is either grown in the presence of lysine or deregulated for lysine biosynthesis.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 15 OF 22 Elsevier BIOBASE COPYRIGHT 2006 Elsevier Science B.V.
on STN DUPLICATE
ACCESSION NUMBER: 2000261887 ESBIOBASE
TITLE: The three-dimensional structure of the ternary complex of *Corynebacterium glutamicum* diaminopimelate dehydrogenase-NADPH-L-2-amino-6-methylene-pimelate
AUTHOR: Cirilli M.; Scapin G.; Sutherland A.; Vederas J.C.; Blanchard J.S.
CORPORATE SOURCE: J.S. Blanchard, Albert Einstein College of Medicine, Department of Biochemistry, Yeshiva University, 1300 Morris Park Avenue, Bronx, NY 10461, United States.
E-mail: blanchar@aecon.yu.edu
SOURCE: Protein Science, (2000), 9/10 (2034-2037), 15 reference(s)
CODEN: PRCIEI ISSN: 0961-8368
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The three-dimensional (3D) structure of *Corynebacterium glutamicum* diaminopimelate D-dehydrogenase in a ternary complex with NADPH and L-2-amino-6-methylene-pimelate has been solved and refined to a resolution of 2.1 Å. L-2-Amino-6-methylene-pimelate was recently synthesized and shown to be a potent competitive inhibitor (5 μM) vs. meso-diaminopimelate of the

Bacillus sphaericus dehydrogenase (Sutherland et al., 1999). Diaminopimelate dehydrogenase catalyzes the reversible NADP.sup.+ -dependent oxidation of the D-amino acid stereocenter of mesodiaminopimelate, and is the only enzyme known to catalyze the oxidative deamination of a D-amino acid. The enzyme is involved in the biosynthesis of meso-diaminopimelate and L-lysine from L-aspartate, a biosynthetic pathway of considerable interest because it is essential for growth of certain bacteria. The dehydrogenase is found in a limited number of species of bacteria, as opposed to the alternative succinylase and acetylase pathways that are widely distributed in bacteria and plants. The structure of the ternary complex reported here provides a structural rationale for the nature and potency of the inhibition exhibited by the unsaturated L-2-amino-6-methylene-pimelate against the dehydrogenase. In particular, we compare the present structure with other structures containing either bound substrate, meso-diaminopimelate, or a conformationally restricted isoxazoline inhibitor. We have identified a significant interaction between the α -L-amino group of the unsaturated inhibitor and the indole ring of Trp144 that may account for the tight binding of this inhibitor.

L5 ANSWER 16 OF 22 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
ACCESSION NUMBER: 1998-379060 [33] WPIDS

DOC. NO. CPI: C2005-242288

TITLE: Recombinant DNA autonomously replicable in coryneform bacteria - used to produce L-lysine, codes for e.g. aspartokinase, di hydropicolinate reductase and synthase and di amino-pimelate decarboxylase.

DERWENT CLASS: B05 C03 D13 D16 E16

INVENTOR(S): ARAKI, M; NAKAMATSU, T; SUGIMOTO, M; YOSHIHARA, Y; YOSHIHA, Y

PATENT ASSIGNEE(S): (AJIN) AJINOMOTO CO INC; (AJIN) AJINOMOTO KK

COUNTRY COUNT: 30

PATENT INFORMATION:

| PATENT NO | KIND | DATE | WEEK | LA | PG |
|--|------|----------|-----------|----|----|
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| EP 854189 | A2 | 19980722 | (199833)* | EN | 59 |
| R: AL AT BE CH DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO | | | | | |
| SK 9701636 | A3 | 19980708 | (199836) | | |
| JP 10215883 | A | 19980818 | (199843) | | 46 |
| HU 9702360 | A2 | 19990628 | (199931) | | |
| BR 9706059 | A | 19991005 | (200006) | | |
| US 6004773 | A | 19991221 | (200006) | | |
| CN 1187540 | A | 19980715 | (200267) | | |
| CN 1524956 | A | 20040901 | (200478) | | |
| HU 224492 | B1 | 20050928 | (200581)B | | |
| CN 1159443 | C | 20040728 | (200612) | | |

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
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| EP 854189 | A2 | EP 1997-121443 | 19971205 |
| SK 9701636 | A3 | SK 1997-1636 | 19971203 |
| JP 10215883 | A | JP 1997-333238 | 19971203 |
| HU 9702360 | A2 | HU 1997-2360 | 19971205 |
| BR 9706059 | A | BR 1997-6059 | 19971205 |
| US 6004773 | A | US 1997-985908 | 19971205 |
| CN 1187540 | A | CN 1997-120820 | 19971205 |
| CN 1524956 | A Div ex | CN 1997-120820 | 19971205 |
| | | CN 2003-133131 | 19971205 |
| HU 224492 | B1 | HU 1997-2360 | 19971205 |

CN 1159443

C

CN 1997-120820

19971205

PRIORITY APPLN. INFO: JP 1996-325659 19961205

AN 1998-379060 [33] WPIDS

AB EP 854189 A UPAB: 20051222

Recombinant DNA (A) autonomously replicable in cells of coryneform bacteria (CB), comprising a DNA sequence coding for an aspartokinase (AK) in which feedback inhibition by L-lysine and L-threonine is desensitised, a DNA sequence coding for a dihydrodipicolinate reductase (DHPR), a DNA sequence coding for dihydropicolic acid synthase (DHPS), a DNA sequence coding for diaminopimelate decarboxylase (DAMD) and a DNA sequence coding for aspartate aminotransferase (AAT), is new.

USE - The DNA and related products can be used for improving L-lysine productivity by CB. The L-lysine produced can be used as a fodder additive.

Dwg. 0/14

L5 ANSWER 17 OF 22 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
ACCESSION NUMBER: 1998-020947 [03] WPIDS

DOC. NO. CPI: C1998-007874

TITLE: Vector containing di amino pimelate decarboxylase and di amino pimelate dehydrogenase genes - used for lysine production by overexpression in coryneform bacteria.

DERWENT CLASS: B05 D16 E16

INVENTOR(S): HAYAKAWA, A; HIRANO, S; IZUI, M; NAKAMATSU, T; NAKANO, E; SUGIMOTO, M; YOSHIHARA, Y; ATSUSHI, H; EIICHI, N; MASAKAZU, S; MASAKO, I; SEIKO, H; TSUYOSHI, N; YASUHIKO, Y

PATENT ASSIGNEE(S): (AJIN) AJINOMOTO CO INC; (AJIN) AJINOMOTO KK

COUNTRY COUNT: 13

PATENT INFORMATION:

| PATENT NO | KIND | DATE | WEEK | LA | PG |
|-------------|-------------|----------|-----------|----|----|
| <hr/> | | | | | |
| EP 811682 | A2 | 19971210 | (199803)* | EN | 63 |
| R: DE DK ES | FR GB IT NL | | | | |
| JP 09322774 | A | 19971216 | (199809) | | 39 |
| SK 9700593 | A3 | 19971210 | (199811) | | |
| BR 9703475 | A | 19980929 | (199846) | | |
| HU 9700851 | A2 | 19990628 | (199931) | | |
| US 6090597 | A | 20000718 | (200037) | | |
| CN 1171442 | A | 19980128 | (200328) | | |
| EP 811682 | B1 | 20040121 | (200410) | EN | |
| R: DE DK ES | FR GB IT NL | | | | |
| DE 69727260 | E | 20040226 | (200419) | | |
| ES 2214567 | T3 | 20040916 | (200462) | | |
| HU 223764 | B1 | 20050128 | (200519) | | |
| SK 284739 | B6 | 20051006 | (200568) | | |

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
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| EP 811682 | A2 | EP 1997-108764 | 19970602 |
| JP 09322774 | A | JP 1996-142812 | 19960605 |
| SK 9700593 | A3 | SK 1997-593 | 19970512 |
| BR 9703475 | A | BR 1997-3475 | 19970605 |
| HU 9700851 | A2 | HU 1997-851 | 19970506 |
| US 6090597 | A | US 1997-852730 | 19970507 |
| CN 1171442 | A | CN 1997-112960 | 19970605 |
| EP 811682 | B1 | EP 1997-108764 | 19970602 |
| DE 69727260 | E | DE 1997-627260 | 19970602 |

| | | | |
|------------|----|----------------|----------|
| ES 2214567 | T3 | EP 1997-108764 | 19970602 |
| HU 223764 | B1 | EP 1997-108764 | 19970602 |
| SK 284739 | B6 | HU 1997-851 | 19970506 |
| | | SK 1997-593 | 19970512 |

FILING DETAILS:

| PATENT NO | KIND | PATENT NO |
|-------------|-------------------|------------|
| DE 69727260 | E Based on | EP 811682 |
| ES 2214567 | T3 Based on | EP 811682 |
| SK 284739 | B6 Previous Publ. | SK 9700593 |

PRIORITY APPLN. INFO: JP 1996-142812 19960605

AN 1998-020947 [03] WPIDS

AB EP 811682 A UPAB: 19980610

A recombinant DNA that is autonomously replicable in cells of coryneform bacteria and comprises a DNA sequence coding for a diaminopimelate decarboxylase and a DNA sequence encoding a diaminopimelate dehydrogenase, is new.

Also claimed is a coryneform bacterium in which the DNA sequence coding for diaminopimelate decarboxylase and the DNA sequence encoding diaminopimelate dehydrogenase are enhanced.

(U)SEU)

The coryneform bacterium is used for producing L-lysine (claimed).
(U)ADVANTAGEU)

Simultaneous overexpression of the diaminopimelate decarboxylase gene (ddc) and the diaminopimelate dehydrogenase gene (lysA) in (IBrevibacterium lactofermentumI) results in increased yields of L-lysine.
(UPREFERRED DNAU)

The diaminopimelate decarboxylase DNA sequence encodes a 445 amino acid sequence given in the specification. The diaminopimelate dehydrogenase DNA sequence encodes a 320 amino acid sequence given in the specification.

(UEXAMPLEU)

Plasmid pDL is a pUC18 derivative containing a ddc insert and a lysA insert. (IB. lactofermentumI) AJ11082 transformed with pDL produced 23.3 g/l of L-lysine after 40 hr and 31.6 g/l after 72 hr. The corresponding values for wild-type AJ11082 were 22.0 and 29.8 g/l.

(GS7)

Dwg. 0/14

L5 ANSWER 18 OF 22 USPATFULL on STN

ACCESSION NUMBER: 92:20924 USPATFULL

TITLE: Cloning of the bioA, bioD, bioF, bioC and BioH genes of bacillus spraericus, vectors and transformed cells

INVENTOR(S): Gloeckler, Remi, Strasbourg, France

Speck, Denis, Eckbolsheim, France

Lemoine, Yves, Strasbourg-Neudorf, France

PATENT ASSIGNEE(S): Transgene S.A., Courbevoie, France (non-U.S. corporation)

| NUMBER | KIND | DATE |
|--------|------|------|
|--------|------|------|

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|---------------------|----------------|--------------|
| PATENT INFORMATION: | US 5096823 | 19920317 |
| APPLICATION INFO.: | US 1987-102740 | 19870930 (7) |

| NUMBER | DATE |
|--------|------|
|--------|------|

| | | |
|-----------------------|---------------|----------|
| PRIORITY INFORMATION: | FR 1986-13603 | 19860930 |
| | FR 1987-6916 | 19870518 |

DOCUMENT TYPE: Utility

FILE SEGMENT: Granted

PRIMARY EXAMINER: Schwartz, Richard A.

ASSISTANT EXAMINER: Nolan, S. L.

LEGAL REPRESENTATIVE: Cushman, Darby & Cushman
NUMBER OF CLAIMS: 21
EXEMPLARY CLAIM: 1, 8
NUMBER OF DRAWINGS: 41 Drawing Figure(s); 38 Drawing Page(s)
LINE COUNT: 814

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates, in particular, to a DNA sequence corresponding to one of the following genes involved in the chain of biotin biosynthesis in bacteria: bioA gene, bioD gene, bioF, bioC and bioH gene.

Vectors containing these sequences enable other microorganisms to be transformed in order to improve the production of biotin.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 19 OF 22 USPATFULL on STN
ACCESSION NUMBER: 89:71975 USPATFULL
TITLE: Coryneform bacteria carrying recombinant plasmids and their use in the fermentative production of L-lysine
INVENTOR(S): Sano, Konosuke, Tokyo, Japan
Ito, Koichi, Kawasaki, Japan
Miwa, Kiyoshi, Matsudo, Japan
Nakamori, Shigeru, Yokohama, Japan
PATENT ASSIGNEE(S): Ajinomoto Company, Inc., Tokyo, Japan (non-U.S. corporation)

| | NUMBER | KIND | DATE |
|-----------------------|--|------|--------------|
| PATENT INFORMATION: | US 4861722 | | 19890829 |
| APPLICATION INFO.: | US 1987-56310 | | 19870601 (7) |
| RELATED APPLN. INFO.: | Continuation of Ser. No. US 1983-525993, filed on 24 Aug 1983, now abandoned | | |
| DOCUMENT TYPE: | Utility | | |
| FILE SEGMENT: | Granted | | |
| PRIMARY EXAMINER: | Moskowitz, Margaret | | |
| LEGAL REPRESENTATIVE: | Oblon, Fisher, Spivak, McClelland & Maier | | |
| NUMBER OF CLAIMS: | 9 | | |
| EXEMPLARY CLAIM: | 1 | | |
| NUMBER OF DRAWINGS: | 9 Drawing Figure(s); 8 Drawing Page(s) | | |
| LINE COUNT: | 537 | | |

AB A genetic sequence coding for the production of a protein having the activity of diaminopimelic acid decarboxylase and having two Pst I cleavage sites in its DNA chain and a molecular weight of 2.9 ± 0.05 Md, is incorporated into a vehicle capable of replication in Coryneform bacteria and used to produce L-lysine by fermentation.

L5 ANSWER 20 OF 22 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
ACCESSION NUMBER: 1985-155057 [26] WPIDS
DOC. NO. CPI: C1985-067542
TITLE: L-Lysine production by fermentation - using Corynebacterium microorganism containing recombinant plasmid with fragment coding for protein which decarbonises di amino-pimelic acid.
DERWENT CLASS: B05 D16 E16
PATENT ASSIGNEE(S): (AJIN) AJINOMOTO KK
COUNTRY COUNT: 3
PATENT INFORMATION:

| PATENT NO | KIND | DATE | WEEK | LA | PG |
|-------------|------|--------------------|------|----|----|
| JP 60062994 | A | 19850411 (198526)* | | 12 | |
| US 4861722 | A | 19890829 (198944) | | | |
| JP 06091829 | B2 | 19941116 (199444) | | 11 | |

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|-------------|------|----------------|----------|
| JP 60062994 | A | JP 1984-169897 | 19840816 |
| US 4861722 | A | US 1987-56310 | 19870601 |
| JP 06091829 | B2 | JP 1984-169897 | 19840816 |

FILING DETAILS:

| PATENT NO | KIND | PATENT NO |
|-------------|-------------|-------------|
| JP 06091829 | B2 Based on | JP 60062994 |

PRIORITY APPLN. INFO: US 1983-525993 19830824; US
1987-56310 19870601

AN 1985-155057 [26] WPIDS

AB JP 60062994 A UPAB: 19930925

Method comprises cultivation of *Corynebacterium* type microorganism which contains a recombinant plasmid having DNA fragment. The fragment has a gene configuration coding information on production of protein having enzymatic activity for decarbonising diamino-pimelic acid, the fragment having mol. weight of 2.9+/-0.5 MD, having 2 PstI sites, 2 Sal I sites, 2 Hind III sites and one Cla I site, and producing small fragments of 1.0MD, 0.7 MD and 0.3 MD, respectively, upon splitting at Pst I site.

0/9

ABEQ US 4861722 A UPAB: 19930925

Corynebacterial and *Brevicatelial* species are transformed with a genetic sequence (obtd. form *Brevibacterium lactofermentum*, ATCC 13,869) which encodes the formation of diaminopimelic acid decarboxylase. The modified bacteria are propagated and the enzyme is isolated from the culture media.

USE - The enzyme is utilised in the prodn. of lysine.

L5 ANSWER 21 OF 22 BIOTECHNO COPYRIGHT 2006 Elsevier Science B.V. on STN
ACCESSION NUMBER: 1984:14163133 BIOTECHNO

TITLE: Purification and characterization of succinyl-CoA:
Tetrahydrodipicolinate N-succinyltransferase from
Escherichia coli

AUTHOR: Simms S.A.; Voige W.H.; Gilvarg C.

CORPORATE SOURCE: Department of Biochemical Sciences, Princeton
University, Princeton, NJ 08544, United States.

SOURCE: Journal of Biological Chemistry, (1984), 259/5
(2734-2741)

CODEN: JBCHA3

DOCUMENT TYPE: Journal; Article

COUNTRY: United States

LANGUAGE: English

AN 1984:14163133 BIOTECHNO

AB Tetrahydrodipicolinate succinylase, an enzyme involved in the diaminopimelate-lysine pathway, was purified 1900-fold from crude extracts of *Escherichia coli*. The enzyme catalyzes the formation of CoA and N-succinyl-2-amino-6-keto-L-pimelate from succinyl-CoA and tetrahydrodipicolinate. The purified enzyme was shown to be homogeneous by polyacrylamide gel electrophoresis. The Stokes radius of the enzyme was determined from its elution volume on a Sephadryl S300 column and its sedimentation constant from sucrose density gradient centrifugation. These were 35 Å and 4.7 (S_{2.3.0.0..w}), respectively. The enzyme consists of two subunits each with a mass of 31,000 daltons, as determined using sodium dodecyl sulfate/polyacrylamide gel electrophoresis.

Tetrahydrodipicolinate succinylase was shown to be a sulfhydryl enzyme. It has a pH optimum of 8.2. The equilibrium lies predominantly in favor of product formation but the reverse reaction can be demonstrated in vitro.

majority of the KAPA was converted to DTB.

L5 ANSWER 15 OF 22 Elsevier BIOBASE COPYRIGHT 2006 Elsevier Science B.V.
on STN

DUPLICATE

AB The three-dimensional (3D) structure of *Corynebacterium glutamicum* diaminopimelate D-dehydrogenase in a ternary complex with NADPH and L-2-amino-6-methylene-pimelate has been solved and refined to a resolution of 2.1 Å. L-2-Amino-6-methylene-pimelate was recently synthesized and shown to be a potent competitive inhibitor (5 µM) vs. meso-diaminopirnate of the *Bacillus sphaericus* dehydrogenase (Sutherland et al., . . . known to catalyze the oxidative deamination of a D-amino acid. The enzyme is involved in the biosynthesis of meso-diaminopimelate and L-lysine from L-aspartate, a biosynthetic pathway of considerable interest because it is essential for growth of certain bacteria. The dehydrogenase is. . . ternary complex reported here provides a structural rationale for the nature and potency of the inhibition exhibited by the unsaturated L-2-amino-6-methylene-pimelate against the dehydrogenase. In particular, we compare the present structure with other structures containing either bound substrate, meso-diaminopimelate, or a. . .

L5 ANSWER 16 OF 22 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN

TI Recombinant DNA autonomously replicable in coryneform bacteria - used to produce L-lysine, codes for e.g. aspartokinase, di hydropicolinate reductase and synthase and di amino-pimelate decarboxylase.

L5 ANSWER 17 OF 22 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN

TI Vector containing di amino pimelate decarboxylase and di amino pimelate dehydrogenase genes - used for lysine production by overexpression in coryneform bacteria.

L5 ANSWER 18 OF 22 USPATFULL on STN

DETD . . . Eisenberg (1985, Annals New York Academy of Sciences 447, 335-349) then proposed that this gene codes for a subunit of pimeloyl-CoA synthetase (bioH). It should be noted that the *E. coli* mutants which are overproductive of biotin (selected either by a level of excretion of vitamin permitting the growth of a bioB auxotroph of *E. coli*, or by resistance to alpha-dehydروبوتين) have all been identified genetically as affected at the bioR locus. This locus codes for a multifunctional protein (repressor of the synthesis of the messenger RNAs of the bioABFCD operon and synthetase holoenzyme binding biotin to a lysine residue of different apoenzymes having a carboxylase function).

L5 ANSWER 19 OF 22 USPATFULL on STN

DETD The biosynthetic pathway for the production of lysine, threonine and isoleucine is shown in the "Description of the Prior Art". The scheme demonstrates the presence of DAPDase enzyme as the last step in the branch leading to L-lysine. DNA containing sufficient genetic information to code for DAPDase is obtained from an appropriate DNA donor. Preferably, the donor is a Coryneform bacterium, most preferably *Brevibacterium lactofermentum*. The genetic information coding for DAPDase can be obtained by partial digestion of DNA from the donor, introduction of the genetic sequence into an appropriate plasmid, transformation of an DAPDase deficient Coryneform bacteria with the resulting mixture of recombinant DNAs, and isolation of transformants which can grow on diamino pimelic acid (dap).

L5 ANSWER 20 OF 22 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN

TT LYSINE PRODUCE FERMENTATION

CORYNEBACTERIUM MICROORGANISM CONTAIN RECOMBINATION PLASMID
FRAGMENT CODE PROTEIN DI AMINO PIMELIC ACID.

AW: DNA ENZYME.

L5 ANSWER 21 OF 22 BIOTECHNO COPYRIGHT 2006 Elsevier Science B.V. on STN
AB Tetrahydrodipicolinate succinylase, an enzyme involved in the
diaminopimelate-lysine pathway, was purified 1900-fold from
crude extracts of *Escherichia coli*. The enzyme
catalyzes the formation of CoA and N-succinyl-2-amino-6-keto-L-
pimelate from succinyl-CoA and tetrahydrodipicolinate. The
purified enzyme was shown to be homogeneous by polyacrylamide gel
electrophoresis. The Stokes radius of . . . shown to be a sulfhydryl
enzyme. It has a pH optimum of 8.2. The equilibrium lies predominantly in
favor of product formation but the reverse reaction can be
demonstrated in vitro.

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(FILE 'HOME' ENTERED AT 21:50:20 ON 16 JUN 2006)

INDEX 'ADISCTI, ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, ANTE, AQUALINE,
AQUASCI, BIOENG, BIOSIS, BIOTECHABS, BIOTECHDS, BIOTECHNO, CABA, CAPLUS,
CEABA-VTB, CIN, CONFSCI, CROPB, CROPU, DDFB, DDFU, DGENE, DISSABS, DRUGB,
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99 FILE TOXCENTER
3167 FILE USPATFULL
294 FILE USPAT2
9 FILE VETU
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L3 11640 SEA LYSI? (S) (PRODUC? OR SYNTHE?) (S) (COLI? OR ESCHERI? OR
BREVIB? OR CORY? OR GLUTAMICU? OR ACTINO? OR ARTHRO?)
L4 31 SEA L3 (S) (PIMEL?)
L5 22 DUP REM L4 (9 DUPLICATES REMOVED)
D TI L5 1-22
D IBIB ABS L5 6-8, 10, 13, 15-21
D KWIC L5 6-8, 10, 13, 15-21

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FILE USPATFULL
FILE COVERS 1971 TO PATENT PUBLICATION DATE: 15 Jun 2006 (20060615/PD)
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ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 15 Jun 2006 (20060615/PD)
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USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Feb 2006

FILE BIOTECHDS
FILE LAST UPDATED: 8 JUN 2006 <20060608/UP>
FILE COVERS 1982 TO DATE

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FILE WPIDS
FILE LAST UPDATED: 16 JUN 2006 <20060616/UP>
MOST RECENT DERWENT UPDATE: 200638 <200638/DW>
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ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 15 Jun 2006 (20060615/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Feb 2006
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Feb 2006

=>
=> s 13(s) (pimel? or diaminopimel?)
L6 424 L3(S) (PIMEL? OR DIAMINOPIMEL?)

=> s 16(s) (anal? or inhibi?)
5 FILES SEARCHED...
L7 221 L6(S) (ANAL? OR INHIBI?)

=> dup rem 17
PROCESSING COMPLETED FOR L7
L8 161 DUP REM L7 (60 DUPLICATES REMOVED)

=> s 18(s) (gene? or dna? or polynucl? or mrna? or cdna?)
3 FILES SEARCHED...
5 FILES SEARCHED...
7 FILES SEARCHED...
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L68(S) (GENE?)'
L9 113 L8(S) (GENE? OR DNA? OR POLYNUCL? OR MRNA? OR CDNA?)

=> d ti l9 1-113

L9 ANSWER 1 OF 113 USPATFULL on STN
TI Intracellular metabolic flux analysis method using substrate labeled
with isotope

L9 ANSWER 2 OF 113 USPATFULL on STN
TI Polynucleotides and polypeptides isolated from lactobacillus and methods
for their use

L9 ANSWER 3 OF 113 USPATFULL on STN
TI Corynebacterium glutamicum genes encoding metabolic pathway proteins

L9 ANSWER 4 OF 113 USPATFULL on STN
TI Corynebacterium glutamicum genes encoding stress, resistance and
tolerance proteins

L9 ANSWER 5 OF 113 USPATFULL on STN
TI Corynebacterium glutamicum genes encoding proteins involved in
homeostasis and adaptation

L9 ANSWER 6 OF 113 USPATFULL on STN
TI Methods and compositions for amino acid production

L9 ANSWER 7 OF 113 USPATFULL on STN
TI Corynebacterium glutamicum genes encoding novel proteins

L9 ANSWER 8 OF 113 USPATFULL on STN
TI Corynebacterium glutamicum genes encoding proteins involved in membrane
synthesis and membrane transport

L9 ANSWER 9 OF 113 USPATFULL on STN
TI Method for determining metabolic flux

L9 ANSWER 10 OF 113 USPATFULL on STN
TI Corynebacterium glutamicum genes encoding phosphoenolpyruvate: sugar
phosphotransferase system proteins

L9 ANSWER 11 OF 113 USPATFULL on STN
TI Corynebacterium glutamicum genes encoding proteins involved in

homeostasis and adaptation

- L9 ANSWER 12 OF 113 USPATFULL on STN
TI Intracellular metabolic flux analysis method using substrate labeled with isotope
- L9 ANSWER 13 OF 113 USPATFULL on STN
TI Attaching substances to microorganisms
- L9 ANSWER 14 OF 113 USPATFULL on STN
TI Corynebacterium glutamicum genes encoding phosphoenolpyruvate: sugar phosphotransferase system proteins
- L9 ANSWER 15 OF 113 USPATFULL on STN
TI Method for producing target substance by fermentation
- L9 ANSWER 16 OF 113 USPATFULL on STN
TI Corynebacterium glutamicum genes encoding proteins involved in homeostasis and adaptation
- L9 ANSWER 17 OF 113 USPATFULL on STN
TI Corynebacterium glutamicum genes encoding stress, resistance and tolerance proteins
- L9 ANSWER 18 OF 113 USPATFULL on STN
TI Method for producing L-lysine using methanol-utilizing bacterium
- L9 ANSWER 19 OF 113 USPATFULL on STN
TI Anti-bacterial methods and materials
- L9 ANSWER 20 OF 113 USPATFULL on STN
TI Genes involved in polysaccharide production and utilization thereof
- L9 ANSWER 21 OF 113 USPATFULL on STN
TI Process for producing l-amino acid and novel gene
- L9 ANSWER 22 OF 113 USPATFULL on STN
TI Process for the production of L-lysine using coryneform bacteria
- L9 ANSWER 23 OF 113 USPATFULL on STN
TI Process for the production of L-lysine using coryneform bacteria
- L9 ANSWER 24 OF 113 USPATFULL on STN
TI Genes of corynebacterium
- L9 ANSWER 25 OF 113 USPATFULL on STN
TI Corynebacterium glutamicum genes encoding proteins involved in membrane synthesis and membrane transport
- L9 ANSWER 26 OF 113 USPATFULL on STN
TI Poroplasts
- L9 ANSWER 27 OF 113 USPATFULL on STN
TI Minicell-based screening for compounds and proteins that modulate the activity of signalling proteins
- L9 ANSWER 28 OF 113 USPATFULL on STN
TI Antibodies to native conformations of membrane proteins
- L9 ANSWER 29 OF 113 USPATFULL on STN
TI Reverse screening and target identification with minicells
- L9 ANSWER 30 OF 113 USPATFULL on STN
TI Minicell-based bioremediation

- L9 ANSWER 31 OF 113 USPATFULL on STN
TI Methods of making pharmaceutical compositions with minicells
- L9 ANSWER 32 OF 113 USPATFULL on STN
TI Minicell-based delivery agents
- L9 ANSWER 33 OF 113 USPATFULL on STN
TI Minicell-based selective absorption
- L9 ANSWER 34 OF 113 USPATFULL on STN
TI Pharmaceutical compositions with minicells
- L9 ANSWER 35 OF 113 USPATFULL on STN
TI Conjugated minicells
- L9 ANSWER 36 OF 113 USPATFULL on STN
TI Methods of minicell-based delivery
- L9 ANSWER 37 OF 113 USPATFULL on STN
TI Minicell-based diagnostics
- L9 ANSWER 38 OF 113 USPATFULL on STN
TI Membrane to membrane delivery
- L9 ANSWER 39 OF 113 USPATFULL on STN
TI Minicell-based gene therapy
- L9 ANSWER 40 OF 113 USPATFULL on STN
TI Solid supports with minicells
- L9 ANSWER 41 OF 113 USPATFULL on STN
TI Minicell libraries
- L9 ANSWER 42 OF 113 USPATFULL on STN
TI Forward screening with minicells
- L9 ANSWER 43 OF 113 USPATFULL on STN
TI Minicell compositions and methods
- L9 ANSWER 44 OF 113 USPATFULL on STN
TI Minicell-based transformation
- L9 ANSWER 45 OF 113 USPATFULL on STN
TI Minicell-producing parent cells
- L9 ANSWER 46 OF 113 USPATFULL on STN
TI Minicell-based rational drug design
- L9 ANSWER 47 OF 113 USPATFULL on STN
TI Target display on minicells
- L9 ANSWER 48 OF 113 USPATFULL on STN
TI Minicell-based transfection
- L9 ANSWER 49 OF 113 USPATFULL on STN
TI Minicells comprising membrane proteins
- L9 ANSWER 50 OF 113 USPATFULL on STN
TI Anti-bacterial methods and materials
- L9 ANSWER 51 OF 113 USPATFULL on STN
TI Polynucleotides and polypeptides, materials incorporating them and methods for using them
- L9 ANSWER 52 OF 113 USPATFULL on STN

- TI *Staphylococcus aureus* polynucleotides and sequences
- L9 ANSWER 53 OF 113 USPATFULL on STN
TI Nucleic acid sequences and expression system relating to *Enterococcus faecium* for diagnostics and therapeutics
- L9 ANSWER 54 OF 113 USPATFULL on STN
TI Method of producing L-lysine
- L9 ANSWER 55 OF 113 USPATFULL on STN
TI *Corynebacterium glutamicum* genes encoding metabolic pathway proteins
- L9 ANSWER 56 OF 113 USPATFULL on STN
TI Novel Polynucleotides
- L9 ANSWER 57 OF 113 USPATFULL on STN
TI Polynucleotides, materials incorporating them, and methods for using them
- L9 ANSWER 58 OF 113 USPATFULL on STN
TI METHOD OF PRODUCING L-LYSINE
- L9 ANSWER 59 OF 113 USPATFULL on STN
TI Method for producing L-lysine
- L9 ANSWER 60 OF 113 USPATFULL on STN
TI Method of producing L-lysine by fermentation
- L9 ANSWER 61 OF 113 USPATFULL on STN
TI Method for producing L-lysine
- L9 ANSWER 62 OF 113 USPATFULL on STN
TI Method of process for producing L-lysine by fermentation
- L9 ANSWER 63 OF 113 USPATFULL on STN
TI Method of inducing lysine overproduction in plants
- L9 ANSWER 64 OF 113 USPATFULL on STN
TI *Bacillus MGA3* aspartokinase II gene
- L9 ANSWER 65 OF 113 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
TI Fermentative preparation of L-lysine-containing product, involves inoculating and culturing bacterium in nutrient medium using coryneform bacteria through oxidative pentose phosphate pathway or tricarboxylic acid cycle;
 involving *Corynebacterium* culture medium optimization for amino acid preparation
- L9 ANSWER 66 OF 113 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
TI Fermentative preparation of L-lysine-containing product by inoculating and culturing coryneform bacteria in nutrient medium, continuously supplying nutrient medium to culture for producing L-lysine, removing culture broth from culture;
 for use in pharmaceutical industry
- L9 ANSWER 67 OF 113 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
TI Fermentative preparation of L-lysine-containing product using coryneform bacteria which produce L-lysine, by culturing bacterium in medium having carbon, nitrogen and phosphorus, and culturing bacterium to allow formation of L-lysine;
 for use in pharmaceutical industry
- L9 ANSWER 68 OF 113 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
TI Fermentative preparation of L-lysine-containing product by inoculating and culturing coryneform bacteria in nutrient medium, continuously

supplying nutrient medium to culture for producing L-lysine, removing culture broth from culture;
for use in pharmaceutical and food industry

- L9 ANSWER 69 OF 113 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
TI Cloning, characterization and heterologous expression of the aspartokinase and aspartate semialdehyde dehydrogenase genes of cephamycin C-producer *Streptomyces clavuligerus*; recombinant enzyme protein purification and characterization via plasmid expression in host cell for use in antibiotic production
- L9 ANSWER 70 OF 113 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
TI Production of L-lysine, comprises fermentation of L-lysine producing coryneform bacteria resistant to diaminopimelic acid analog, enrichment of L-lysine in medium, isolation of L-lysine or its feedstuffs additive from fermentation broth; involving culture medium optimization and fermentation
- L9 ANSWER 71 OF 113 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
TI Producing L-lysine by fermenting L-lysine producing coryneform bacteria sensitive to 4-hydroxydiaminopimelate, adding L-lysine in medium/bacterial cell, optionally isolating L-lysine/L-lysine-containing feedstuff additive; involving *Corynebacterium glutamicum* fermentation
- L9 ANSWER 72 OF 113 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
TI Producing target substance e.g. L-amino acid, by culturing a mutant or recombinant microorganism in a culture medium to produce and accumulate target substance, and collecting target substance from the culture; L-amino acid production by recombinant *Escherichia coli* culture
- L9 ANSWER 73 OF 113 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
TI New bacterium of genus *Escherichia*, for producing L-threonine, is available in conjunction with two strains of *Escherichia coli*, and subsequent mutation and selection of aminohydroxyvaleric acid negative strains; L-amino acid production by *Escherichia* sp. culture, useful as food and food-additive, and in medicine
- L9 ANSWER 74 OF 113 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
TI New recombinant DNA encoding aspartokinase in Coryneform bacterium; recombinant aspartate-kinase used in preparation of L-lysine
- L9 ANSWER 75 OF 113 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
TI Recombinant DNA autonomously replicable in coryneform bacteria; used to produce L-lysine, codes for e.g. aspartokinase, dihydropicolinate-reductase and synthase and diaminopimelate-decarboxylase
- L9 ANSWER 76 OF 113 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
TI Dynamics of intracellular flux distribution at branchpoints in *Corynebacterium* metabolism; metabolic engineering for e.g. amino acid production (conference abstract)
- L9 ANSWER 77 OF 113 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
TI L-lysine production by culture of transformant *Corynebacterium*; *Brevibacterium lactofermentum* recombinant aspartokinase expression in *B. lactofermentum* using vector plasmid pCAB, for reduced feedback inhibition
- L9 ANSWER 78 OF 113 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
TI L-lysine production by culture of transformant *Corynebacterium*; *Brevibacterium lactofermentum* recombinant aspartokinase expression in *B. lactofermentum* using vector plasmid pCAB, for reduced feedback

- inhibition
- L9 ANSWER 79 OF 113 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
TI Construction of L-lysine, L-threonine-, or L-isoleucine-overproducing
strains of *Corynebacterium glutamicum*;
metabolic engineering for strain improvement (conference paper)
- L9 ANSWER 80 OF 113 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
TI Metabolic design in amino acid producing bacterium *Corynebacterium glutamicum*;
metabolic engineering; a review (conference paper)
- L9 ANSWER 81 OF 113 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
TI Production of L-lysine by culture of *Escherichia coli* transformant;
dihydrodipicolinate-reductase and diaminopimelate-dehydrogenase
expression in *E. coli*, for application in recombinant L-lysine production
- L9 ANSWER 82 OF 113 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
TI Effect of different levels of aspartokinase on the lysine production by
Corynebacterium lactofermentum;
transconjugation and electroporation; sequence analysis of the
beta-subunit
- L9 ANSWER 83 OF 113 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
TI Cloning and sequence analysis of the meso-diaminopimelate-decarboxylase
gene from *Bacillus methanolicus* MGA3 and comparison to other
decarboxylase genes;
gene cloning and expression in *Escherichia coli* for use in L-lysine preparation
- L9 ANSWER 84 OF 113 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
TI Control of the lysine biosynthesis sequence in *Corynebacterium glutamicum* as analyzed by overexpression of the individual corresponding genes;
feedback inhibition resistant aspartate-kinase and
dihydrodipicolinate-synthase gene cloning and expression
- L9 ANSWER 85 OF 113 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
TI Cloning and expression of key enzymes in L-lysine biosynthesis from
thermophilic bacilli: diaminopimelate-decarboxylase from *Bacillus MGA3*;
gene cloning in *Escherichia coli* (conference abstract)
- L9 ANSWER 86 OF 113 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
TI Cloning and expression of *lysA* gene in *Escherichia coli* and
Brevibacterium flavum;
diaminopimelate-decarboxylase gene containing shuttle vector plasmid
pCW1 construction (conference abstract)
- L9 ANSWER 87 OF 113 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
TI Cloning and sequencing of the meso-diaminopimelate-D-dehydrogenase (ddh)
gene of *Corynebacterium glutamicum*;
involved in lysine biosynthesis
- L9 ANSWER 88 OF 113 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
TI General organization of the genes specifically involved in the
diaminopimelate-lysine biosynthetic pathway of *Corynebacterium glutamicum*;
diaminopimelate-synthase, diaminopimelate-decarboxylase and
tetrahydropimelate-synthetase gene localization
- L9 ANSWER 89 OF 113 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
TI Regulation of lysine biosynthesis in *Brevibacterium flavum*;
enzyme activities measured in extracts from 2 lysine producing strains
- L9 ANSWER 90 OF 113 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN

- TI New dapC gene from coryneform bacteria, useful when over-expressed for increasing fermentative production of L-amino acids, and also for isolating related sequences.
- L9 ANSWER 91 OF 113 LIFESCI COPYRIGHT 2006 CSA on STN
TI MosA, a Protein Implicated in Rhizopine Biosynthesis in Sinorhizobium meliloti L5-30, is a Dihydrodipicolinate Synthase
- L9 ANSWER 92 OF 113 LIFESCI COPYRIGHT 2006 CSA on STN
TI The Lysis Protein E of Phi X174 Is a Specific Inhibitor of the MraY-catalyzed Step in Peptidoglycan Synthesis
- L9 ANSWER 93 OF 113 LIFESCI COPYRIGHT 2006 CSA on STN
TI Expression in Escherichia coli, purification and kinetic analysis of the aspartokinase and aspartate semialdehyde dehydrogenase from the rifamycin SV-producing Amycolatopsis mediterranei U32
- L9 ANSWER 94 OF 113 LIFESCI COPYRIGHT 2006 CSA on STN
TI Characterization of the Sinorhizobium meliloti genes encoding a functional dihydrodipicolinate synthase (dapA) and dihydrodipicolinate reductase (dapB)
- L9 ANSWER 95 OF 113 LIFESCI COPYRIGHT 2006 CSA on STN
TI The Dual Biosynthetic Capability of N-Acetylornithine Aminotransferase in Arginine and Lysine Biosynthesis
- L9 ANSWER 96 OF 113 LIFESCI COPYRIGHT 2006 CSA on STN
TI Identification and transcriptional analysis of the dapB-ORF2-dapA-ORF4 operon of Corynebacterium glutamicum, encoding two enzymes involved in L-lysine synthesis
- L9 ANSWER 97 OF 113 LIFESCI COPYRIGHT 2006 CSA on STN
TI Molecular genetic analysis of the region containing the essential Pseudomonas aeruginosa asd gene encoding aspartate- beta -semialdehyde dehydrogenase
- L9 ANSWER 98 OF 113 LIFESCI COPYRIGHT 2006 CSA on STN
TI Metabolic design in the amino-acid-producing bacterium Corynebacterium glutamicum
- L9 ANSWER 99 OF 113 LIFESCI COPYRIGHT 2006 CSA on STN
TI A study on the mechanism of action of sceptrin, an antimicrobial agent isolated from the South Pacific sponge Agelas mauritiana
- L9 ANSWER 100 OF 113 LIFESCI COPYRIGHT 2006 CSA on STN
TI Analysis of different DNA fragments of Corynebacterium glutamicum complementing dapE of Escherichia coli
- L9 ANSWER 101 OF 113 LIFESCI COPYRIGHT 2006 CSA on STN
TI The essential Escherichia coli msgB gene, a multicopy suppressor of a temperature-sensitive allele of the heat shock gene grpE, is identical to dapE.
- L9 ANSWER 102 OF 113 LIFESCI COPYRIGHT 2006 CSA on STN
TI Regulation of enzymes of lysine biosynthesis in Corynebacterium glutamicum
- L9 ANSWER 103 OF 113 LIFESCI COPYRIGHT 2006 CSA on STN
TI Chromosomal location and nucleotide sequence of the Escherichia coli dapA gene.
- L9 ANSWER 104 OF 113 LIFESCI COPYRIGHT 2006 CSA on STN
TI Expression of genes of Bacillus subtilis lysine biosynthesis in Escherichia coli cells.

L9 ANSWER 105 OF 113 Elsevier BIOBASE COPYRIGHT 2006 Elsevier Science B.V.
on STN
TI Pathway analysis and metabolic engineering in *Corynebacterium glutamicum*

L9 ANSWER 106 OF 113 Elsevier BIOBASE COPYRIGHT 2006 Elsevier Science B.V.
on STN
TI Site-specific inactivation of meso-Diaminopimelate-dehydrogenase
gene (ddh) in a lysine-producing *Brevibacterium lactofermentum*

L9 ANSWER 107 OF 113 Elsevier BIOBASE COPYRIGHT 2006 Elsevier Science B.V.
on STN
TI Synthesis and testing of heterocyclic analogues of diaminopimelic acid
(DAP) as inhibitors of DAP dehydrogenase and DAP epimerase

L9 ANSWER 108 OF 113 BIOTECHNO COPYRIGHT 2006 Elsevier Science B.V. on STN
TI Molecular aspects of lysine, threonine, and isoleucine biosynthesis in
Corynebacterium glutamicum

L9 ANSWER 109 OF 113 BIOTECHNO COPYRIGHT 2006 Elsevier Science B.V. on STN
TI Attachment of diaminopimelic acid to bdelloplast peptidoglycan during
intraperiplasmic growth of *Bdellovibrio bacteriovorus* 109J

L9 ANSWER 110 OF 113 CAPLUS COPYRIGHT 2006 ACS on STN
TI Production of L-lysine in genetically engineered coryneform bacteria

L9 ANSWER 111 OF 113 CAPLUS COPYRIGHT 2006 ACS on STN
TI The expression of *Escherichia coli* diaminopimelate decarboxylase in mouse
3T3 cells

L9 ANSWER 112 OF 113 USPAT2 on STN
TI *Staphylococcus aureus* polynucleotides and sequences

L9 ANSWER 113 OF 113 USPAT2 on STN
TI Methods for monitoring multiple gene expression

=> d ibib abs 19 7-8, 16 20 21-22, 24, 54 55 58-63, 68, 70-71, 75 78 84 87 102 105
106-108, 110

L9 ANSWER 7 OF 113 USPATFULL on STN
ACCESSION NUMBER: 2005:283230 USPATFULL
TITLE: *Corynebacterium glutamicum* genes encoding novel
proteins
INVENTOR(S): Pompejus, Markus, Freinsheim, GERMANY, FEDERAL REPUBLIC
OF
Kroger, Burkhard, Limburgerhof, GERMANY, FEDERAL
REPUBLIC OF
Schroder, Hartwig, Nussloch, GERMANY, FEDERAL REPUBLIC
OF
Zelder, Oskar, Speyer, GERMANY, FEDERAL REPUBLIC OF
Haberhauer, Gregor, Limburgerhof, GERMANY, FEDERAL
REPUBLIC OF
PATENT ASSIGNEE(S): BASF Aktiengesellschaft, Ludwigshafen, GERMANY, FEDERAL
REPUBLIC OF (non-U.S. corporation)

| | NUMBER | KIND | DATE |
|---------------------|----------------|------|--------------|
| PATENT INFORMATION: | US 6962989 | B1 | 20051108 |
| APPLICATION INFO.: | US 2000-605703 | | 20000627 (9) |

| | NUMBER | DATE |
|-----------------------|-----------------|---------------|
| PRIORITY INFORMATION: | US 1999-152318P | 19990903 (60) |
| | US 1999-142764P | 19990708 (60) |
| DOCUMENT TYPE: | Utility | |

FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Moran, Marjorie
LEGAL REPRESENTATIVE: Lahive & Cockfield, LLP, Hanley, Elizabeth A.,
Laccotripe Zacharakis, Maria

NUMBER OF CLAIMS: 5
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 0 Drawing Figure(s); 0 Drawing Page(s)
LINE COUNT: 16658

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Isolated nucleic acid molecules, designated MCP nucleic acid molecules, which encode novel MCP proteins from *Corynebacterium glutamicum* are described. The invention also provides antisense nucleic acid molecules, recombinant expression vectors containing MCP nucleic acid molecules, and host cells into which the expression vectors have been introduced. The invention still further provides isolated MCP proteins, mutated MCP proteins, fusion proteins, antigenic peptides and methods for the improvement of production of a desired compound from *C. glutamicum* based on genetic engineering of MCP genes in this organism.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L9 ANSWER 8 OF 113 USPATFULL on STN
ACCESSION NUMBER: 2005:280984 USPATFULL
TITLE: *Corynebacterium glutamicum* genes encoding proteins involved in membrane synthesis and membrane transport
INVENTOR(S): Pompejus, Markus, Freinsheim, GERMANY, FEDERAL REPUBLIC OF
Kroger, Burkhard, Limburgerhof, GERMANY, FEDERAL REPUBLIC OF
Schroder, Hartwig, Nussloch, GERMANY, FEDERAL REPUBLIC OF
Zelder, Oskar, Speyer, GERMANY, FEDERAL REPUBLIC OF
Haberhauer, Gregor, Limburgerhof, GERMANY, FEDERAL REPUBLIC OF
PATENT ASSIGNEE(S): BASF AG, Ludwigshafen, DE, UNITED STATES (non-U.S. corporation)

| | NUMBER | KIND | DATE |
|-----------------------|--|------|---------------|
| PATENT INFORMATION: | US 2005244935 | A1 | 20051103 |
| APPLICATION INFO.: | US 2005-82389 | A1 | 20050316 (11) |
| RELATED APPLN. INFO.: | Continuation of Ser. No. US 2000-603024, filed on 23 Jun 2000, PENDING | | |

| | NUMBER | DATE |
|-----------------------|------------------|---------------|
| PRIORITY INFORMATION: | DE 1999-19930487 | 19990701 |
| | DE 1999-19930489 | 19990701 |
| | DE 1999-19931549 | 19990708 |
| | DE 1999-19931550 | 19990708 |
| | DE 1999-19932134 | 19990709 |
| | DE 1999-19941379 | 19990831 |
| | DE 1999-19942088 | 19990903 |
| | DE 1999-19942097 | 19990903 |
| | US 1999-141031P | 19990625 (60) |
| | US 1999-143262P | 19990709 (60) |
| | US 1999-151281P | 19990827 (60) |

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: LAHIVE & COCKFIELD, LLP., 28 STATE STREET, BOSTON, MA, 02109, US
NUMBER OF CLAIMS: 22
EXEMPLARY CLAIM: 1
LINE COUNT: 11811
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Isolated nucleic acid molecules, designated MCT nucleic acid molecules, which encode novel MCT proteins from *Corynebacterium glutamicum* are described. The invention also provides antisense nucleic acid molecules, recombinant expression vectors containing MCT nucleic acid molecules, and host cells into which the expression vectors have been introduced. The invention still further provides isolated MCT proteins, mutated MCT proteins, fusion proteins, antigenic peptides and methods for the improvement of production of a desired compound from *C. glutamicum* based on genetic engineering of MCT genes in this organism.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L9 ANSWER 16 OF 113 USPATFULL on STN
ACCESSION NUMBER: 2004:317313 USPATFULL
TITLE: *Corynebacterium glutamicum* genes encoding proteins involved in homeostasis and adaptation
INVENTOR(S): Pompejus, Markus, Freinsheim, GERMANY, FEDERAL REPUBLIC OF
Kroger, Burkhard, Limburgerhof, GERMANY, FEDERAL REPUBLIC OF
Schroder, Hartwig, Nussloch, GERMANY, FEDERAL REPUBLIC OF
Zelder, Oskar, Speyer, GERMANY, FEDERAL REPUBLIC OF
Haberhauer, Gregor, Limburgerhof, GERMANY, FEDERAL REPUBLIC OF
PATENT ASSIGNEE(S): BASF Aktiengesellschaft, GERMANY, FEDERAL REPUBLIC OF (non-U.S. corporation)

| | NUMBER | KIND | DATE |
|---------------------|----------------|------|--------------|
| PATENT INFORMATION: | US 6831165 | B1 | 20041214 |
| APPLICATION INFO.: | US 2000-602777 | | 20000623 (9) |

| | NUMBER | DATE |
|-----------------------|--|---------------|
| PRIORITY INFORMATION: | US 1999-141031P | 19990625 (60) |
| DOCUMENT TYPE: | Utility | |
| FILE SEGMENT: | GRANTED | |
| PRIMARY EXAMINER: | Horlick, Kenneth R. | |
| ASSISTANT EXAMINER: | Wilder, Cynthia | |
| LEGAL REPRESENTATIVE: | Lahive & Cockfield LLP, Hanley, Elizabeth A., DiRocco, Lisa M. | |
| NUMBER OF CLAIMS: | 15 | |
| EXEMPLARY CLAIM: | 1 | |
| NUMBER OF DRAWINGS: | 0 Drawing Figure(s); 0 Drawing Page(s) | |
| LINE COUNT: | 5143 | |

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Isolated nucleic acid molecules, designated HA nucleic acid molecules, which encode novel HA proteins from *Corynebacterium glutamicum* are described. The invention also provides antisense nucleic acid molecules, recombinant expression vectors containing HA nucleic acid molecules, and host cells into which the expression vectors have been introduced. The invention still further provides isolated HA proteins, mutated HA proteins, fusion proteins, antigenic peptides and methods for the improvement of production of a desired compound from *C. glutamicum* based on genetic engineering of HA genes in this organism.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L9 ANSWER 20 OF 113 USPATFULL on STN
ACCESSION NUMBER: 2004:215462 USPATFULL
TITLE: Genes involved in polysaccharide production and utilization thereof
INVENTOR(S): Asahara, Takayuki, Kawasaki, JAPAN
Yasueda, Hisashi, Kawasaki, JAPAN

| | NUMBER | KIND | DATE |
|---------------------|----------------|------|---------------|
| PATENT INFORMATION: | US 2004166570 | A1 | 20040826 |
| APPLICATION INFO.: | US 2004-772271 | A1 | 20040206 (10) |

| | NUMBER | DATE |
|-----------------------|---|----------|
| PRIORITY INFORMATION: | JP 2003-32075 | 20030210 |
| DOCUMENT TYPE: | Utility | |
| FILE SEGMENT: | APPLICATION | |
| LEGAL REPRESENTATIVE: | AJINOMOTO CORPORATE SERVICES, LLC, INTELLECTUAL PROPERTY DEPARTMENT, 1120 CONNECTICUT AVE., N.W., WASHINGTON, DC, 20036 | |

NUMBER OF CLAIMS: 9
EXEMPLARY CLAIM: 1
LINE COUNT: 1180

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB An ability of a methanol-utilizing bacterium to produce a polysaccharide is improved or suppressed using a DNA encoding a protein selected from the group consisting of:

- (A) a protein which has the amino acid sequence of SEQ ID NO: 2;
- (B) a variant of a protein which has the amino acid sequence of SEQ ID NO: 2 comprising substitution, deletion, insertion or addition of one or several amino acid residues and has an activity for producing a polysaccharide;
- (C) a protein which has the amino acid sequence of SEQ ID NO: 4; and
- (D) a variant of a protein which has the amino acid sequence of SEQ ID NO: 4 comprising substitution, deletion, insertion or addition of one or several amino acid residues and has an activity for producing a polysaccharide.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L9 ANSWER 21 OF 113 USPATFULL on STN
ACCESSION NUMBER: 2004:158629 USPATFULL
TITLE: Process for producing l-amino acid and novel gene
INVENTOR(S): Sugimoto, Masakazu, Kawasaki-shi, JAPAN
Nakai, Yuta, Kawasaki-shi, JAPAN
Ito, Hisao, Kawasaki-shi, JAPAN
Kurahashi, Osamu, Kawasaki-shi, JAPAN

| | NUMBER | KIND | DATE |
|---------------------|----------------|------|---------------|
| PATENT INFORMATION: | US 2004121428 | A1 | 20040624 |
| APPLICATION INFO.: | US 2002-148898 | A1 | 20020619 (10) |
| | WO 2000-JP9164 | | 20001222 |

| | NUMBER | DATE |
|-----------------------|--|----------|
| PRIORITY INFORMATION: | JP 1999-368096 | 19991224 |
| DOCUMENT TYPE: | Utility | |
| FILE SEGMENT: | APPLICATION | |
| LEGAL REPRESENTATIVE: | OBLON, SPIVAK, MCCLELLAND, MAIER & NEUSTADT, P.C., 1940 DUKE STREET, ALEXANDRIA, VA, 22314 | |
| NUMBER OF CLAIMS: | 10 | |
| EXEMPLARY CLAIM: | 1 | |
| LINE COUNT: | 1205 | |

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A gene coding for fructose phosphotransferase is introduced into a coryneform bacterium having an ability to produce an L-amino acid such

as L-lysine or L-glutamic acid to enhance fructose phosphotransferase activity and thereby improve the L-amino acid producing ability.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L9 ANSWER 22 OF 113 USPATFULL on STN
ACCESSION NUMBER: 2004:88592 USPATFULL
TITLE: Process for the production of L-lysine using coryneform bacteria
INVENTOR(S): Bathe, Brigitte, Salzkotten, GERMANY, FEDERAL REPUBLIC OF
Hans, Stephan, Osnabrueck, GERMANY, FEDERAL REPUBLIC OF
Pfefferle, Walter, Halle, GERMANY, FEDERAL REPUBLIC OF
PATENT ASSIGNEE(S): Degussa AG, Duesseldorf, GERMANY, FEDERAL REPUBLIC OF,
D-40474 (non-U.S. corporation)

| | NUMBER | KIND | DATE |
|---------------------|----------------|------|---------------|
| PATENT INFORMATION: | US 2004067562 | A1 | 20040408 |
| APPLICATION INFO.: | US 2003-630740 | A1 | 20030731 (10) |

| | NUMBER | DATE |
|-----------------------|---|---------------|
| PRIORITY INFORMATION: | DE 2002-10235028 | 20020731 |
| | US 2002-401751P | 20020808 (60) |
| DOCUMENT TYPE: | Utility | |
| FILE SEGMENT: | APPLICATION | |
| LEGAL REPRESENTATIVE: | OBLON, SPIVAK, MCCLELLAND, MAIER & NEUSTADT, P.C., 1940
DUKE STREET, ALEXANDRIA, VA, 22314 | |

NUMBER OF CLAIMS: 21
EXEMPLARY CLAIM: 1
LINE COUNT: 530

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A process for the production of L-lysine, in which the following steps are carried out:

- a) fermentation of the L-lysine producing coryneform bacteria that are at least resistant to diaminopimelic acid analogues, in particular 4-hydroxydiaminopimelic acid;
- b) enrichment of the L-lysine in the medium or in the bacterial cells; and optionally
- c) isolation of the L-lysine or L-lysine-containing feedstuffs additive from the fermentation broth, so that ≥0 to 100% of the constituents from the fermentation broth and/or from the biomass are present,

and optionally bacteria are used in which in addition further genes of the biosynthesis pathway of L-lysine are enhanced, or bacteria are used in which the metabolic pathways that reduce the formation of L-lysine are at least partially switched off.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L9 ANSWER 24 OF 113 USPATFULL on STN
ACCESSION NUMBER: 2004:57946 USPATFULL
TITLE: Genes of corynebacterium
INVENTOR(S): Pompejus, Markus, Freinsheim, GERMANY, FEDERAL REPUBLIC OF
Kroger, Burkhard, Limburgerhof, GERMANY, FEDERAL REPUBLIC OF
Zelder, Oskar, Speyer, GERMANY, FEDERAL REPUBLIC OF
Schroder, Hartwig, Nubloch, GERMANY, FEDERAL REPUBLIC OF

| | NUMBER | KIND | DATE |
|-----------------------|--|------|---------------|
| PATENT INFORMATION: | US 2004043953 | A1 | 20040304 |
| APPLICATION INFO.: | US 2003-450055 | A1 | 20030610 (10) |
| | WO 2000-EP13143 | | 20001222 |
| DOCUMENT TYPE: | Utility | | |
| FILE SEGMENT: | APPLICATION | | |
| LEGAL REPRESENTATIVE: | NIXON & VANDERHYE, PC, 1100 N GLEBE ROAD, 8TH FLOOR, ARLINGTON, VA, 22201-4714 | | |
| NUMBER OF CLAIMS: | 37 | | |
| EXEMPLARY CLAIM: | 1 | | |
| LINE COUNT: | 6534 | | |

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Isolated nucleic acid molecules, designated MP nucleic acid molecules, which encode novel MP proteins from *Corynebacterium glutamicum* are described. The invention also provides antisense nucleic acid molecules, recombinant expression vectors containing MP nucleic acid molecules, and host cells into which the expression vectors have been introduced. The invention still further provides isolated MP proteins, mutated MP proteins, fusion proteins, antigenic peptides and methods for the improvement of production of a desired compound from *C. glutamicum* based on genetic engineering of MP genes in this organism.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

| | | |
|---------------------|---|--------|
| L9 ANSWER 54 OF 113 | USPATFULL | on STN |
| ACCESSION NUMBER: | 2003:78586 USPATFULL | |
| TITLE: | Method of producing L-lysine | |
| INVENTOR(S): | Otsuna, Seiko, Kawasaki-shi, JAPAN | |
| | Sugimoto, Masakazu, Kawasaki-shi, JAPAN | |
| | Izui, Masako, Kawasaki-shi, JAPAN | |
| | Hayakawa, Atsushi, Kawasaki-shi, JAPAN | |
| | Nakano, Eiichi, Kawasaki-shi, JAPAN | |
| | Kobayashi, Masaki, Kawasaki-shi, JAPAN | |
| | Yoshihara, Yasuhiko, Kawasaki-shi, JAPAN | |
| | Nakamatsu, Tsuyoshi, Kawasaki-shi, JAPAN | |
| PATENT ASSIGNEE(S): | AJINOMOTO CO. INC., Tokyo, JAPAN, 104-8315 (non-U.S. corporation) | |

| | NUMBER | KIND | DATE |
|-----------------------|--|------|---------------|
| PATENT INFORMATION: | US 2003054506 | A1 | 20030320 |
| APPLICATION INFO.: | US 2002-226136 | A1 | 20020823 (10) |
| RELATED APPLN. INFO.: | Continuation of Ser. No. US 1997-952976, filed on 8 Dec 1997, ABANDONED A 371 of International Ser. No. WO 1996-JP1511, filed on 5 Jun 1996, UNKNOWN | | |

| | NUMBER | DATE |
|-----------------------|---|----------|
| PRIORITY INFORMATION: | JP 1995-140614 | 19950607 |
| DOCUMENT TYPE: | Utility | |
| FILE SEGMENT: | APPLICATION | |
| LEGAL REPRESENTATIVE: | OBLON SPIVAK MCCLELLAND MAIER & NEUSTADT PC, FOURTH FLOOR, 1755 JEFFERSON DAVIS HIGHWAY, ARLINGTON, VA, 22202 | |
| NUMBER OF CLAIMS: | 18 | |
| EXEMPLARY CLAIM: | 1 | |
| NUMBER OF DRAWINGS: | 14 Drawing Page(s) | |
| LINE COUNT: | 2278 | |

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The L-lysine-producing ability and the L-lysine-producing speed are improved in a coryneform bacterium harboring an aspartokinase in which feedback inhibition by L-lysine and L-threonine is

substantially desensitized, by successively enhancing DNA coding for a dihydronicotinate reductase, DNA coding for a dihydronicotinate synthase, DNA coding for a diaminopimelate decarboxylase, and DNA coding for a diaminopimelate dehydrogenase.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L9 ANSWER 55 OF 113 USPATFULL on STN
ACCESSION NUMBER: 2003:71519 USPATFULL
TITLE: Corynebacterium glutamicum genes encoding metabolic pathway proteins
INVENTOR(S): Pompejus, Markus, Freinsheim, GERMANY, FEDERAL REPUBLIC OF
Kroger, Burkhard, Limburgerhof, GERMANY, FEDERAL REPUBLIC OF
Schroder, Hartwig, Nussloch, GERMANY, FEDERAL REPUBLIC OF
Zelder, Oskar, Speyer, GERMANY, FEDERAL REPUBLIC OF
Haberhauer, Gregor, Limburgerhof, GERMANY, FEDERAL REPUBLIC OF
Kim, Jun-Won, Seoul, KOREA, REPUBLIC OF
Lee, Heung-Shick, Seoul, KOREA, REPUBLIC OF
Hwang, Byung-Joon, Seoul, KOREA, REPUBLIC OF

| | NUMBER | KIND | DATE |
|-----------------------|---|------|--------------|
| PATENT INFORMATION: | US 2003049804 | A1 | 20030313 |
| APPLICATION INFO.: | US 2000-746660 | A1 | 20001222 (9) |
| RELATED APPLN. INFO.: | Continuation-in-part of Ser. No. US 2000-606740, filed on 23 Jun 2000, PENDING Continuation-in-part of Ser. No. US 2000-603124, filed on 23 Jun 2000, PENDING | | |

| | NUMBER | DATE |
|-----------------------|------------------|---------------|
| PRIORITY INFORMATION: | DE 1999-19931420 | 19990708 |
| | US 1999-141031P | 19990625 (60) |
| | US 1999-142101P | 19990702 (60) |
| | US 1999-148613P | 19990812 (60) |
| | US 2000-187970P | 20000309 (60) |

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: LAHIVE & COCKFIELD, 28 STATE STREET, BOSTON, MA, 02109
NUMBER OF CLAIMS: 47
EXEMPLARY CLAIM: 1
LINE COUNT: 15004

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Isolated nucleic acid molecules, designated MP nucleic acid molecules, which encode novel MP proteins from *Corynebacterium glutamicum* are described. The invention also provides antisense nucleic acid molecules, recombinant expression vectors containing MP nucleic acid molecules, and host cells into which the expression vectors have been introduced. The invention still further provides isolated MP proteins, mutated MP proteins, fusion proteins, antigenic peptides and methods for the improvement of production of a desired compound from *C. glutamicurn* based on genetic engineering of MP genes in this organism.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L9 ANSWER 58 OF 113 USPATFULL on STN
ACCESSION NUMBER: 2002:164752 USPATFULL
TITLE: METHOD OF PRODUCING L-LYSINE
INVENTOR(S): OTSUNA, SEIKO, KAWASAKI-SHI, JAPAN
SUGIMOTO, MASAKAZU, KAWASAKI-SHI, JAPAN
IZUI, MASAKO, KAWASAKI-SHI, JAPAN

HAYAKAWA, ATSUSHI, KAWASAKI-SHI, JAPAN
NAKANO, EIICHI, KAWASAKI-SHI, JAPAN
KOBAYASHI, MASAKI, KAWASAKI-SHI, JAPAN
YOSHIHARA, YASUHIKO, KAWASAKI-SHI, JAPAN
NAKAMATSU, TSUYOSHI, KAWASAKI-SHI, JAPAN

| | NUMBER | KIND | DATE |
|---------------------|----------------|------|--------------|
| PATENT INFORMATION: | US 2002086370 | A1 | 20020704 |
| APPLICATION INFO.: | US 1997-952976 | A1 | 19971208 (8) |
| | WO 1996-JP1511 | | 19960605 |

| | NUMBER | DATE |
|-----------------------|---|----------|
| PRIORITY INFORMATION: | JP 1995-140614 | 19950607 |
| DOCUMENT TYPE: | Utility | |
| FILE SEGMENT: | APPLICATION | |
| LEGAL REPRESENTATIVE: | OBLON SPIVAK MCCLELLAND MAIER & NEUSTADT PC, FOURTH FLOOR, 1755 JEFFERSON DAVIS HIGHWAY, ARLINGTON, VA, 22202 | |

NUMBER OF CLAIMS: 18
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 14 Drawing Page(s)
LINE COUNT: 2281

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The L-lysine-producing ability and the L-lysine-producing speed are improved in a coryneform bacterium harboring an aspartokinase in which feedback inhibition by L-lysine and L-threonine is substantially desensitized, by successively enhancing DNA coding for a dihydroadipic acid reductase, DNA coding for a dihydroadipic acid synthase, DNA coding for a diaminopimelate decarboxylase, and DNA coding for a diaminopimelate dehydrogenase.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L9 ANSWER 59 OF 113 USPATFULL on STN
ACCESSION NUMBER: 2001:59658 USPATFULL
TITLE: Method for producing L-lysine
INVENTOR(S): Hayakawa, Atsushi, Kawasaki, Japan
Sugimoto, Masakazu, Kawasaki, Japan
Yoshihara, Yasuhiko, Kawasaki, Japan
Nakamatsu, Tsuyoshi, Kawasaki, Japan
PATENT ASSIGNEE(S): Ajinomoto Co., Inc., Tokyo, Japan (non-U.S. corporation)

| | NUMBER | KIND | DATE |
|---------------------|----------------|------|--------------|
| PATENT INFORMATION: | US 6221636 | B1 | 20010424 |
| APPLICATION INFO.: | US 1997-985916 | | 19971205 (8) |

| | NUMBER | DATE |
|-----------------------|---|----------|
| PRIORITY INFORMATION: | JP 1996-325658 | 19961205 |
| DOCUMENT TYPE: | Utility | |
| FILE SEGMENT: | Granted | |
| PRIMARY EXAMINER: | Stole, Einar | |
| LEGAL REPRESENTATIVE: | Oblon, Spivak, McClelland, Maier & Neustadt, P.C. | |
| NUMBER OF CLAIMS: | 22 | |
| EXEMPLARY CLAIM: | 1 | |
| NUMBER OF DRAWINGS: | 13 Drawing Figure(s); 13 Drawing Page(s) | |
| LINE COUNT: | 1291 | |

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A recombinant DNA autonomously replicable in cells of

coryneform bacteria, comprising a DNA sequence coding for an aspartokinase in which feedback inhibition by L-lysine and L-threonine is substantially desensitized, and a DNA sequence coding for a diaminopimelate decarboxylase; a coryneform bacterium harboring an aspartokinase in which feedback inhibition by L-lysine and L-threonine is substantially desensitized, and comprising an enhanced DNA sequence coding for a diaminopimelate decarboxylase; and a method for producing L-lysine comprising the steps of cultivating the coryneform bacterium in an appropriate medium to allow L-lysine to be produced and accumulated in a culture of the bacterium, and collecting L-lysine from the culture.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L9 ANSWER 60 OF 113 USPATFULL on STN
ACCESSION NUMBER: 2000:34406 USPATFULL
TITLE: Method of producing L-lysine by fermentation
INVENTOR(S): Kojima, Hiroyuki, Kawasaki, Japan
Ogawa, Yuri, Kawasaki, Japan
Kawamura, Kazue, Kawasaki, Japan
Sano, Konosuke, Kawasaki, Japan
PATENT ASSIGNEE(S): Ajinomoto Co., Inc., Tokyo, Japan (non-U.S.
corporation)

| | NUMBER | KIND | DATE |
|---------------------|----------------|------|--------------------------|
| PATENT INFORMATION: | US 6040160 | | 20000321 |
| | WO 9516042 | | 19950615 |
| APPLICATION INFO.: | US 1996-648010 | | 19960529 (8) |
| | WO 1994-JP1994 | | 19941128 |
| | | | 19960529 PCT 371 date |
| | | | 19960529 PCT 102(e) date |

| | NUMBER | DATE |
|-----------------------|---|----------|
| PRIORITY INFORMATION: | JP 1993-308397 | 19931208 |
| DOCUMENT TYPE: | Utility | |
| FILE SEGMENT: | Granted | |
| PRIMARY EXAMINER: | Sisson, Bradley | |
| ASSISTANT EXAMINER: | Stole, Einar | |
| LEGAL REPRESENTATIVE: | Oblon, Spivak, McClelland, Maier & Neustadt, P.C. | |
| NUMBER OF CLAIMS: | 22 | |
| EXEMPLARY CLAIM: | 1 | |
| NUMBER OF DRAWINGS: | 24 Drawing Figure(s); 18 Drawing Page(s) | |
| LINE COUNT: | 3168 | |

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A bacterium belonging to the genus *Escherichia*, which is transformed by introducing, into its cells, a DNA coding for a dihydronicotinate synthase originating from a bacterium belonging to the genus *Escherichia* having mutation to desensitize feedback inhibition by L-lysine and a DNA coding for an aspartokinase III originating from a bacterium belonging to the genus *Escherichia* having mutation to desensitize feedback inhibition by L-lysine; preferably a bacterium belonging to the genus *Escherichia* in which a dihydronicotinate reductase gene and a diaminopimelate dehydrogenase gene originating from *Brevibacterium lactofermentum* (or a succinyl diaminopimelate transaminase gene and a succinyl diaminopimelate deacylase gene) are further enhanced, is cultivated in an appropriate medium, L-lysine is produced and accumulated in a culture thereof, and L-lysine is collected from the culture.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L9 ANSWER 61 OF 113 USPATFULL on STN
ACCESSION NUMBER: 1999:166814 USPATFULL
TITLE: Method for producing L-lysine
INVENTOR(S): Araki, Masayuki, Kawasaki, Japan
Sugimoto, Masakazu, Kawasaki, Japan
Yoshihara, Yasuhiko, Kawasaki, Japan
Nakamatsu, Tsuyoshi, Kawasaki, Japan
PATENT ASSIGNEE(S): Ajinomoto Co., Inc., Tokyo, Japan (non-U.S.
corporation)

| | NUMBER | KIND | DATE |
|---------------------|----------------|------|--------------|
| PATENT INFORMATION: | US 6004773 | | 19991221 |
| APPLICATION INFO.: | US 1997-985908 | | 19971205 (8) |

| | NUMBER | DATE |
|-----------------------|---|----------|
| PRIORITY INFORMATION: | JP 1996-325659 | 19961205 |
| DOCUMENT TYPE: | Utility | |
| FILE SEGMENT: | Granted | |
| PRIMARY EXAMINER: | Degen, Nancy | |
| LEGAL REPRESENTATIVE: | Oblon, Spivak, McClelland, Maier & Neustadt, P.C. | |
| NUMBER OF CLAIMS: | 12 | |
| EXEMPLARY CLAIM: | 1 | |
| NUMBER OF DRAWINGS: | 14 Drawing Figure(s); 13 Drawing Page(s) | |
| LINE COUNT: | 2900 | |

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A coryneform bacterium harboring an aspartokinase in which feedback inhibition by L-lysine and L-threonine is substantially desensitized, and comprising an enhanced DNA sequence coding for a dihydrodipicolinate reductase, an enhanced DNA sequence coding for dihydropicolic acid reductase, an enhanced DNA sequence coding for dihydropicolic acid synthase, an enhanced DNA sequence coding for diaminopimelate decarboxylase and an enhanced DNA sequence coding for aspartate aminotransferase; a method for producing L-lysine comprising the steps of cultivating the coryneform bacterium in an appropriate medium to allow L-lysine to be produced and accumulated in a culture of the bacterium, and collecting L-lysine from the culture; and a recombinant DNA usable for production of the coryneform bacterium.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L9 ANSWER 62 OF 113 USPATFULL on STN
ACCESSION NUMBER: 1999:150978 USPATFULL
TITLE: Method of process for producing L-lysine by fermentation
INVENTOR(S): Kojima, Hiroyuki, Kawasaki, Japan
Ogawa, Yuri, Kawasaki, Japan
Kawamura, Kazue, Kawasaki, Japan
Sano, Konosuke, Kawasaki, Japan
PATENT ASSIGNEE(S): Ajinomoto Co., Inc., Tokyo, Japan (non-U.S.
corporation)

| | NUMBER | KIND | DATE |
|---------------------|----------------|------|-----------------------|
| PATENT INFORMATION: | US 5989875 | | 19991123 |
| | WO 9641871 | | 19961227 |
| APPLICATION INFO.: | US 1998-973461 | | 19980420 (8) |
| | WO 1996-JP648 | | 19960314 |
| | | | 19980420 PCT 371 date |

19980420 PCT 102(e) date

| | NUMBER | DATE |
|-----------------------|---|----------|
| PRIORITY INFORMATION: | JP 1995-146054 | 19950613 |
| DOCUMENT TYPE: | Utility | |
| FILE SEGMENT: | Granted | |
| PRIMARY EXAMINER: | Wax, Robert A. | |
| ASSISTANT EXAMINER: | Mayhew, Bradley S. | |
| LEGAL REPRESENTATIVE: | Oblon, Spivak, McClelland, Maier & Neustadt, P.C. | |
| NUMBER OF CLAIMS: | 14 | |
| EXEMPLARY CLAIM: | 1 | |
| NUMBER OF DRAWINGS: | 10 Drawing Figure(s); 9 Drawing Page(s) | |
| LINE COUNT: | 1977 | |

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A bacterium belonging to the genus *Serratia*, which is transformed by introducing into its cells, a DNA coding for a dihydrodipicolinate synthase originating from a bacterium belonging to the genus *Escherichia* or *Serratia* having mutation to desensitize feedback inhibition by L-lysine and a DNA coding for an aspartokinase originating from a bacterium belonging to the genus *Escherichia* or *Serratia* having mutation to desensitize feedback inhibition by L-lysine is cultivated in an appropriate medium, L-lysine is produced and accumulated in a culture thereof, and L-lysine is collected from the culture.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L9 ANSWER 63 OF 113 USPATFULL on STN
ACCESSION NUMBER: 93:91554 USPATFULL
TITLE: Method of inducing lysine overproduction in plants
INVENTOR(S): Glassman, Kimberly F., Minneapolis, MN, United States
Barnes, Linda J., Ames, IA, United States
Pilacinski, William P., Maple Grove, MN, United States
PATENT ASSIGNEE(S): Molecular Genetics Research and Development Limited
Partnership, Minneapolis, MN, United States (U.S.
corporation)

| | NUMBER | KIND | DATE |
|-----------------------|---|------|--------------|
| PATENT INFORMATION: | US 5258300 | | 19931102 |
| APPLICATION INFO.: | US 1988-204388 | | 19880609 (7) |
| DOCUMENT TYPE: | Utility | | |
| FILE SEGMENT: | Granted | | |
| PRIMARY EXAMINER: | Chereskin, Che S. | | |
| LEGAL REPRESENTATIVE: | Merchant, Gould, Smith, Edell, Welter & Schmidt | | |
| NUMBER OF CLAIMS: | 16 | | |
| EXEMPLARY CLAIM: | 9 | | |
| NUMBER OF DRAWINGS: | 2 Drawing Figure(s); 3 Drawing Page(s) | | |
| LINE COUNT: | 1098 | | |

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A method is provided for increasing the level of free L-lysine in a plant comprising: (a) introducing a foreign gene into the cells of a plant tissue source; and (b) expressing said foreign gene in said cells, wherein a first DNA sequence of said gene encodes dihydrosyphenylalanine (DHDPS) which is substantially resistant to feedback inhibition by endogenously-produced free L-lysine.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L9 ANSWER 68 OF 113 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
ACCESSION NUMBER: 2005-11410 BIOTECHDS
TITLE: Fermentative preparation of L-lysine-containing product by inoculating and culturing coryneform bacteria in nutrient medium, continuously supplying nutrient medium to culture for producing L-lysine, removing culture broth from culture;

for use in pharmaceutical and food industry

AUTHOR: GERIGK M; HERMANN T; BATHE B; KELLE R
PATENT ASSIGNEE: DEGUSSA AG
PATENT INFO: WO 2005021772 10 Mar 2005
APPLICATION INFO: WO 2004-EP8882 7 Aug 2004
PRIORITY INFO: US 2003-499710 4 Sep 2003; DE 2003-1039847 29 Aug 2003
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2005-214583 [22]

AN 2005-11410 BIOTECHDS
AB DERWENT ABSTRACT:

NOVELTY - Fermentative preparation (M1) of an L-lysine-containing product using coryneform bacteria which produce L-lysine, involves inoculating and culturing the bacterium in a first nutrient medium, continuously providing further nutrient medium or media to the culture, where the nutrient medium comprises carbon, nitrogen and phosphorus source, and removing the culture broth from the culture.

DETAILED DESCRIPTION - Fermentative preparation (M1) of an L-lysine-containing product using coryneform bacteria which produce L-lysine, involves (a) inoculating and culturing the bacterium in at least a first nutrient medium, and (b) continuously providing at least a further nutrient medium or further nutrient media to the culture in one or several feed streams, under conditions which allow the formation of L-lysine, where the nutrient medium or the nutrient media comprises at least one source of carbon, at least one source of nitrogen and at least one source of phosphorus, and at the same time culture broth is removed from the culture with at least one or several removal streams, which substantially corresponds/respond to the feed stream or the total of the feed streams, where over the entire period of time of the providing step, a concentration of the source(s) of carbon of not more than 10 g/l is established, and over the entire period of time of the providing step, the formation of L-lysine, based on lysine hydrochloride, takes place with an output index (OI)=space/time yield (g/(lxh))xyield(w/w)xconcentration of lysine hydrochloride (g/l) of at least 130 g2/(l2xh).

BIOTECHNOLOGY - Preferred Method: In (M1), the culturing step is carried out by the batch process (batch) or by the feed process (fed batch), in which at least one additional nutrient medium is employed. The source of carbon is one or more of the compounds chosen from sucrose, molasses from sugar beet or cane sugar, fructose, glucose, starch hydrolysate, maltose, xylose, acetic acid, ethanol and methanol. The source of nitrogen is one or more of organic nitrogen-containing substances or their mixtures chosen from peptones, yeast extracts, meat extracts, malt extracts, corn steep liquor, soya bean flour and urea and/or one or more of the inorganic compounds chosen from ammonia, ammonium-containing salts and salts of nitric acid. The ammonium-containing salts and salts of nitric acid are ammonium sulfate, ammonium chloride, ammonium phosphate, ammonium carbonate, ammonium nitrate, potassium nitrate and potassium sodium nitrate. The source of phosphorus is alkali metal or alkaline earth metal salts of phosphoric acid or their polymers, or of phytic acid. The alkali metal salts of phosphoric acid are potassium dihydrogen phosphate or dipotassium hydrogen phosphate or the corresponding sodium-containing salts. The feed stream established in step (b) or the sum of the feed streams is fed in at a rate corresponding to an average residence time of at most 60, at most 55, at most 50, at most 45, at most 35 or at most 30 hours. The average residence time is at most 35 hours. The rate of the removal stream or the removal streams corresponds to 80-120%, preferably 90-110% of the feed stream or of the sum of the feed streams. The concentration of the source of carbon over the entire period of time of step (b) and/or in the case of prior culturing in the feed process (fed batch), also during the feeding of the additional nutrient medium is not more than 10, 5 or 3 g/l. The culture broth removed is provided with oxygen or an

oxygen-containing gas until the concentration of the source of carbon is not more than 2 g/l, not more than 1 g/l or not more than 0.5 g/l. The yield of the L-lysine-containing product is (in weight%) (at least 43 or 48) based on the sugar employed. The space/time yield is 2.5 or 3.5 g/(lxh) or more. The concentration of the lysine hydrochloride in the fermentation broth led off is at least 100, at least 110, at least 120, at least 130 or at least 140 g/l. The formation of the L-lysine, based on lysine hydrochloride, takes place with an output index (OI) of at least 170 or 200 g2/(12xh). The step (b) is carried out for more than 100 or 200 hours. The nutrient media employed in the step (a) or (b) comprise complex constituents chosen from peptones, yeast extracts, meat extracts, malt extracts, corn steep liquor and soya bean flour. The nutrient media comprises complex constituents (in weight%) (5). The L-lysine-containing fermentation broth led off has an osmolarity of not more than 2100, 1800, 1500 or 1200 mosm/l. The L-lysine-containing fermentation broth produced and led off is prepared as a liquid product with 0-100% of the biomass formed in the fermentation after a 10-90% dewatering. The coryneform bacterium contains at least one lysC gene or allele, which codes for an aspartate kinase that is insensitive towards inhibition by lysine or mixtures of lysine and threonine. The L-lysine-producing coryneform bacteria have one or more of the features chosen from lysC allele (lysCfbr), hom allele (homleaky), zwf allele, coding for an NADPH-insensitive glucose 6-phosphate dehydrogenase, and pyc allele, coding for a pyruvate carboxylase. The L-lysine-producing coryneform bacterium has one or more resistances chosen from azauracilr (Azar), rifamycinr (Rifr) and streptomycinr (Strepr). The L-lysine-producing coryneform bacterium has (a) 2 copies of an lysC allele (lysCfbr), a hom allele (homleaky) and 2 copies of a zwf allele, which codes for an NADPH-insensitive glucose 6-phosphate dehydrogenase, or (b) one or more of 3, 4 or 5 copies of an lysC allele (lysCfbr), 2 copies of an lysE gene, and 2 copies of a zwal gene. The L-lysine-producing coryneform bacterium is sensitive towards diaminopimelic acid analogs chosen from 4-hydroxy-diaminopimelic acid, 4-fluoro-diaminopimelic acid, 4-oxo-diaminopimelic acid and 2,4,6-triaminopimelic acid, preferably 4-hydroxy-diaminopimelic acid. The L-lysine-producing coryneform bacterium has the ability to divert the carbon flow through the oxidative pentose phosphate pathway with a percentage content of more than 75%, 85%, 95%, 105%, 115%, 125%, 135% or 145%. The L-lysine-producing coryneform bacterium has the ability to divert the carbon flow through the anaplerotic reactions, based on the sum of pyruvate and phosphoenol pyruvate (PEP), which are converted into oxaloacetate by PEP carboxylase and pyruvate carboxylase, respectively, coded by ppc and pyc, respectively, with a percentage content of more than 19%, 23%, 26%, 28%, 30%, 33%, 35%, or 37%. The L-lysine-producing coryneform bacterium has the ability to divert the carbon flow into the tricarboxylic acid cycle, based on the acetyl radicals, which are transferred from acetyl-CoA to oxaloacetate by the citrate synthase reaction, with a percentage content of at least 1% but not more than 20%, at least 2% but not more than 18%, or at least 3% but not more than 16%. The L-lysine-producing coryneform bacterium has the ability to divert the carbon flow through the lysine-resistant aspartate kinase, coded by lysC, with a percentage content of at least 28% but not more than 56%, at least 30% but not more than 54%, at least 32% but not more than 52% or at least 33% but not more than 50%. The L-lysine-producing coryneform bacterium has the ability to divert the carbon flow through diaminopimelate dehydrogenase, coded by ddh, with a percentage content of at least 49% but not more than 98%, at least 53% but not more than 95%, at least 56% but not more than 91% or at least 58% but not more than 87%. The L-lysine-producing

coryneform bacterium has the ability to establish a ratio of the carbon flow through the oxidative pentose phosphate pathway to the carbon flow through the anaplerotic reactions (oxidative pentose phosphate pathway (%)/anaplerotic reactions (%)=PPP/Ana (-)) of at least 3.4 but not more than 4.6, at least 3.5 but not more than 4.5, at least 3.6 but not more than 4.4, or at least 3.7 but not more than 4.3. The L-lysine-producing **coryneform** bacterium has the ability to establish a ratio of the carbon flow through the oxidative pentose phosphate pathway to the carbon flow into the tricarboxylic acid cycle (oxidative pentose phosphate pathway (%)/tricarboxylic acid cycle (%)=PPP/TCA (-)) of at least 7 but not more than 150, at least 10 but not more than 125, at least 13 but not more than 100 or at least 16 but not more than 75. The L-lysine contained in the fermentation broth is removed and purified. The fermentation broth led off has a solid content (in weight%) (at least 10, 12.5, 15 or at least 17.5). The fermentation broth led off is concentrated by the removal of water, to obtain L-lysine-containing product comprising lysine (in weight%) (35-80), protein (maximum 7), carboxylic acids (maximum 7), total sugars (maximum 9), fats and oils (maximum 5) and minerals (3-30). After dewatering, the L-lysine-containing product has a water content (in weight%) (at least 0.5, but not more than 5.0). The concentration of the by-product trehalose, ketoglutarate, succinate, malate, oxaloacetate, acetate and pyruvate in the fermentation broth led off is not more than 10, 5, 2 or 0.5 g/l. The concentration of the by-product lactate and ethanol in the fermentation broth led off is not more than 8, 4, 2 or 0.5 g/l. The concentration of the by-product L-alanine and L-valine in the fermentation broth led off is not more than 5, 2.5, 1 or 0.25 g/l. The concentration of the by-product L-glutamate in the fermentation broth led off is not more than 7.5, 5, 2 or 0.5 g/l. The L-lysine-containing fermentation broth led off has a total by-product concentration of not more than 2.5%, 1% or 0.5%. After dewatering and granulation, the L-lysine-containing product has an average particle size of 0.1-1.0 mm, 97%, 98% or more. The L-lysine-containing product has a lactate content (in weight%) (not more than 3, 2, 1, 0.5, or 0.1). After dewatering and granulation, the L-lysine-containing product has bulk density of at least 600 kg/m³, 650 kg/m², 700 kg/m³, or at least 750 kg/m³. After dewatering and granulation, the L-lysine-containing product contains a content of additive added, in particular oil (in weight%) (0.02-2), based on the total amount of L-lysine-containing product, on the surface. The L-lysine-containing product contains as an additive one or more of oils chosen from mineral oil, vegetable oils, soya oil, olive oil, soya/lecithin mixtures, edible oils, mixtures of vegetable oils, on the surface.

USE - (M1) is useful for fermentative preparation of an L-lysine-containing product using **coryneform** bacteria such as *Corynebacterium* (claimed). The L-lysine produced by (M1) is useful in pharmaceutical industry, foodstuffs industry and in animal nutrition.

ADVANTAGE - (M1) enables improved fermentative production of L-lysine. (40 pages)

L9 ANSWER 70 OF 113 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
ACCESSION NUMBER: 2004-09352 BIOTECHDS
TITLE: Production of L-lysine, comprises fermentation of L-lysine producing coryneform bacteria resistant to diaminopimelic acid analog, enrichment of L-lysine in medium, isolation of L-lysine or its feedstuffs additive from fermentation broth; involving culture medium optimization and fermentation
AUTHOR: BATHE B; HANS S; PFEFFERLE W
PATENT ASSIGNEE: DEGUSSA AG
PATENT INFO: WO 2004013341 12 Feb 2004
APPLICATION INFO: WO 2003-EP7474 10 Jul 2003

PRIORITY INFO: DE 2002-1035028 31 Jul 2002; DE 2002-1035028 31 Jul 2002
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2004-191378 [18]
AN 2004-09352 BIOTECHDS
AB DERWENT ABSTRACT:

NOVELTY - Production (M1) of L-lysine, involves fermentation of the L-lysine producing coryneform bacteria that are at least resistant to diaminopimelic acid analog, in particular 4-hydroxydiaminopimelic acid, enrichment of the L-lysine in the medium or in the bacterial cells, and optionally, isolation of the L-lysine or L-lysine-containing feedstuffs additive from the fermentation broth.

DETAILED DESCRIPTION - Production (M1) of L-lysine , involves fermentation of the L-lysine producing coryneform bacteria that are at least resistant to diaminopimelic acid analog, in particular 4-hydroxydiaminopimelic acid, enrichment of the L-lysine in the medium or in the bacterial cells, and optionally, isolation of the L-lysine or L-lysine-containing feedstuffs additive from the fermentation broth, such that at least 0-100% of the constituents from the fermentation broth and/or from the biomass are present.

INDEPENDENT CLAIMS are also included for the following: (1) mutants of coryneform bacteria producing L-lysine and that are resistant to one or more of the diaminopimelic acid analogs chosen from 4-fluorodiamino-pimelic acid, 4-hydroxydiaminopimelic acid, 4-oxo-diaminopimelic acid or 2,4,6-triaminopimelic acid; and (2) feedstuffs additives based on fermentation broth, comprising L-lysine produced by (M1) and biomass and/or constituents from the fermentation broth formed during the fermentation of the L-lysine-producing microorganisms in an amount of 0-5% or 90-100%.

BIOTECHNOLOGY - Preferred Method: In (M1), the bacteria used comprises genes of the biosynthesis pathway of L-lysine are enhanced. The bacteria are used in which the metabolic pathways that reduce the formation of L-lysine are at least partially switched off. The production of L-lysine

coryneform microorganisms are fermented in which at the same time one or more of the genes chosen from following group is/are enhanced, in particular overexpressed: the gene lysC coding for a feedback-resistant aspartate kinase, the gene dapA coding for dihydrodipicolinate synthase, the gene gap coding for glyceraldehyde-3-phosphate dehydrogenase, the gene pyc coding for pyruvate carboxylase, the gene zwf coding for glucose-6-phosphate dehydrogenase, simultaneously the gene lysE coding for the lysine export protein, the gene zwal coding for the Zwal protein, the gene lysA coding for diaminopimelic acid decarboxylase, the gene sigC coding for the sigma factor C, the gene tpi coding for triose phosphate isomerase, or the gene pgk coding for 3-phosphoglycerate kinase. The production of L-lysine

coryneform microorganisms are fermented in which at the same time one or more of the genes chosen from the following group is/are attenuated: the pck gene coding for phosphoenol pyruvate carboxykinase, the pgi gene coding for glucose-6-phosphate-isomerase, the gene dead coding for DNA helicase, the gene citE coding for citrate lysase, the gene menE coding for O-succinylbenzoic acid CoA-ligase, the gene mikE17 coding for the transcription regulator Mike17, the gene poxB coding for pyruvate oxidase, or the gene zwa2 coding for the Zwa2 protein. The mutants of coryneform bacteria are used that produce L-lysine and that are resistant to one or more of the diaminopimelic acid analogs.

USE - (M1) is useful for producing L-lysine,

where the microorganisms of the species *Corynebacterium glutamicum* are used that are resistant to 4-hydroxydiaminopimelic acid (claimed).

ADVANTAGE - (M1) is an improved process for the fermentative production of L-lysine.

EXAMPLE - To produce L-lysine, the following test was done. The *Corynebacterium glutamicum* strain DSM 15662Hdapr obtained was cultured in a nutrient medium suitable for the production of lysine and the lysine content in the culture supernatant was determined. The strains were first of all incubated on agar plates for 24 hours at 33 degrees C. Using this agar plate culture a preculture was inoculated (10 ml of medium in a 100 ml Erlenmeyer flask). The medium MM was used as medium for the preculture. The preculture was incubated for 24 hours at 33 degrees C at 240 rpm on a vibrator. Using this preculture a main culture was inoculated such that the initial optical density (OD-660 nm) of the main culture was 0.1 OD. The medium MM was also used for the main culture. Culturing was carried out in a 10 ml volume in a 100 ml Erlenmeyer flask equipped with baffles. The culturing was carried out at 33 degrees C and 80% atmospheric humidity. After 72 hour, the OD was determined at a measurement wavelength of 660 nm with a Biomek 1000 instrument. The amount of lysine formed was determined by ion exchange chromatography and post-column derivatisation with ninhydrin detection, using an amino acid analyzer from Eppendorf-BioTronik. The result showed that high levels of L-lysine was produced by DSM 15662Hdapr (18.9 g/l) than the control DSM 15662 (16.2 g/l). (25 pages)

L9 ANSWER 71 OF 113 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. ON STN
ACCESSION NUMBER: 2004-08783 BIOTECHDS

TITLE: Producing L-lysine by fermenting L-lysine producing coryneform bacteria sensitive to 4-hydroxydiaminopimelate, adding L-lysine in medium/bacterial cell, optionally isolating L-lysine/L-lysine-containing feedstuff additive; involving *Corynebacterium glutamicum* fermentation

AUTHOR: BATHE B; REYNEN C; PFEFFERLE W

PATENT ASSIGNEE: DEGUSSA AG

PATENT INFO: WO 2004013340 12 Feb 2004

APPLICATION INFO: WO 2003-EP7475 10 Jul 2003

PRIORITY INFO: DE 2002-1035029 31 Jul 2002; DE 2002-1035029 31 Jul 2002

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: WPI: 2004-157137 [15]

AN 2004-08783 BIOTECHDS

AB DERWENT ABSTRACT:

NOVELTY - Producing (M1) L-lysine by fermenting L-lysine producing coryneform bacteria that are at least sensitive to diaminopimelate analogues, preferably 4-hydroxydiaminopimelate, enriching L-lysine in medium or in bacterial cells, and optionally, isolating L-lysine or L-lysine-containing feedstuffs additive from fermentation broth, where /- 0 to 100% of constituents from the fermentation broth and/or from biomass are present.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (1) mutants of coryneform bacteria producing L-lysine and that are sensitive to one or more of the diaminopimelate analogues chosen from 4-fluorodiaminopimelate, 4-oxo-diaminopimelate and 2,4,6-triaminopimelate; and (2) feedstuffs additives based on fermentation broth, containing L-lysine produced by (M1), the biomass and/or constituents from the fermentation broth formed during the fermentation of the L-lysine-producing microorganisms in an amount of 0-5% or 90-100%.

BIOTECHNOLOGY - Preferred Method: In (M1), the bacteria used for producing L-lysine, contains enhanced additional

genes of the biosynthesis pathway of L-lysine or metabolic pathways that reduce the formation of L-lysine in bacteria are at least partially switched off. The production of L-lysine by coryneform microorganisms are fermented in which at the same time one or more genes is/are enhanced, preferably overexpressed, where the enhanced gene is chosen from the gene lysC coding for a feedback-resistant aspartate kinase, the gene dapA coding for dihydridopicolinate synthase, the gene gap coding for glyceraldehyde-3-phosphate dehydrogenase, the gene pyc coding for pyruvate carboxylase, the gene zwf coding for glucose-6-phosphate dehydrogenase, simultaneously the gene lysE coding for the lysine export protein, the gene zwal coding for the Zwal protein, the gene lysA coding for diaminopimelate decarboxylase, the gene sigC coding for the sigma factor C, the gene tpi coding for triose phosphate isomerase and the gene pgk coding for 3-phosphoglycerate kinase, or one or more genes is/are attenuated, where the attenuated gene is chosen from the pck gene coding for phosphoenol pyruvate carboxykinase, pgi gene coding for glucose-6-phosphate-isomerase, gene deaD coding for DNA helicase, gene citE coding for citrate lysase, gene menE coding for O-succinylbenzoic acid CoA-ligase, gene mikE17 coding for the transcription regulator MikE17, gene poxB coding for pyruvate oxidase and gene zwa2 coding for the Zwa2 protein. The microorganism producing L-lysine is *Corynebacterium glutamicum*, which is sensitive to 4-hydroxydiaminopimelate.

USE - (M1) Is useful for producing L-lysine by *Corynebacterium glutamicum*, which is sensitive to 4-hydroxydiaminopimelate (claimed).

ADVANTAGE - (M1) Is efficient in producing L-lysine by *Corynebacterium glutamicum*, which is sensitive to 4-hydroxydiaminopimelate.

EXAMPLE - *Corynebacterium glutamicum* strain DSM13994 was produced by multiple, untargeted mutagenesis, of *C. glutamicum* ATCC13032. The mutant sensitive to 4-hydroxydiaminopimelate were screened by plating *C. glutamicum* DSM13994 on LB agar plates containing 10 g/l of 4-hydroxydiaminopimelate. The growth of the colonies were observed over 48 hours. At this concentration mutants sensitive to 4-hydroxydiaminopimelate was differentiated from the unaltered parent strain by a delayed growth. A clone was identified as DSM13994Hdaps, that exhibited a substantially delayed growth compared to DSM13994. The obtained *C. glutamicum* strain DSM13994Haps was cultured in medium MM containing 5 g/l of corn steep liquor (CSL), 20 g/l of morpholinopropanesulfonate (MOPS), 50 g/l of glucose, 25 g/l of diammonium sulfate, 0.1 g/l of potassium dihydrogen phosphate, 1.0 g/l of magnesium sulfate, 10 mg/l calcium chloride, 10 mg/l ferrous sulfate, 5.0 mg/l manganese sulfate, 0.3 mg/l biotin, 0.2 mg/l of thiamine, 25 g/l calcium carbonate for 24 hours at 33 degreesC. Using the agar plate culture, a preculture was inoculated in 100 ml medium MM and incubated for 24 hours at 33 degreesC at 240 rpm on a vibrator. Then main culture was inoculated and incubated so that the initial optimal density (OD-660 nm) of the main culture was 0.1 OD. After 72 hours, the OD and the amount of lysine formed was determined by ion exchange chromatography. On analysis, DSM13994 produced 18.9 g/l of lysine while DSM13994Hdaps produced 19.6 g/l of lysine efficiently. (22 pages)

L9 ANSWER 75 OF 113 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
ACCESSION NUMBER: 1998-09269 BIOTECHDS

TITLE: Recombinant DNA autonomously replicable in coryneform bacteria;

used to produce L-lysine, codes for e.g. aspartokinase, dihydridopicolinate-reductase and synthase and diaminopimelate-decarboxylase

AUTHOR: Araki M; Sugimoto M; Yoshihara Y; Nakamatsu T
PATENT ASSIGNEE: Ajinomoto
LOCATION: Tokyo, Japan.
PATENT INFO: EP 854189 22 Jul 1998
APPLICATION INFO: EP 1997-121443 5 Dec 1997
PRIORITY INFO: JP 1996-325659 5 Dec 1996
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 1998-379060 [33]
AN 1998-09269 BIOTECHDS
AB A recombinant DNA autonomously replicable in cells of *coryneform* bacteria (CB) is claimed comprising a DNA sequence encoding: an aspartokinase (EC-2.7.2.4) (AK) in which feedback inhibition by L-lysine and L-threonine is desensitized; a dihydronicotinate-reductase (EC-1.3.1.26) (DHPR); a dihydronicotinate-synthase (EC-4.2.1.52) (DHPS); a diaminopimelate-decarboxylase (EC-4.1.1.20) (DAMD); and an aspartate-aminotransferase (EC-2.6.1.10) (AAT). Also claimed is: (a) a CB harbouring an AK in which feedback inhibition by L-lysine and L-threonine is desensitized, comprising enhanced DNA sequences coding for DHPR, DHPS, DAMD and AAT; producing L-lysine by culturing CB as in (a) in an appropriate medium to produce, accumulate and collect L-lysine; DNA coding for a protein of disclosed protein sequence; and a vector plasmid pVK7 which is autonomously replicable in cells of *Escherichia coli* and *Brevibacterium lactofermentum*, and comprising a multiple cloning site and lacZ. The products can be used for improving L-lysine productivity by CB. The L-lysine produced can be used as a feed-additive. (59pp)

L9 ANSWER 78 OF 113 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. ON STN
ACCESSION NUMBER: 1997-02208 BIOTECHDS
TITLE: L-lysine production by culture of transformant
Corynebacterium; *Brevibacterium lactofermentum* recombinant aspartokinase expression in *B. lactofermentum* using vector plasmid pCAB, for reduced feedback inhibition
AUTHOR: Otsuna S; Sugimoto M; Izui M; Hayakawa A; Nakano E; Kobayashi M; Yoshihara Y; Nakamatsu T
PATENT ASSIGNEE: Ajinomoto
LOCATION: Tokyo, Japan.
PATENT INFO: WO 9640934 19 Dec 1996
APPLICATION INFO: WO 1996-JP1511 5 Jun 1996
PRIORITY INFO: JP 1995-140614 7 Jun 1995
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
OTHER SOURCE: WPI: 1997-052331 [05]
AN 1997-02208 BIOTECHDS
AB A new recombinant DNA sequence functional in *Corynebacterium* contains DNA encoding an aspartokinase (EC-2.7.2.4) in which feedback inhibition by L-lysine and L-threonine has been substantially reduced, together with DNA encoding for dihydronicotinate-reductase. At least 1 of the following may also be present: DNA encoding dihydronicotinate-synthase; DNA encoding diaminopimelate-decarboxylase (EC-4.1.1.20); or DNA encoding diaminopimelate -dehydrogenase (EC-1.4.1.16). Preferably, the aspartokinase is derived from *Brevibacterium lactofermentum* (ATCC 13869) aspartokinase (of specified DNA sequence). Preferred DNA sequences for the reductase, synthase, decarboxylase, and dehydrogenase are specified. Also claimed are *Corynebacterium* hosts transformed with the above DNA, and the production of L-lysine by culture of the transformants. L-lysine production by fermentation with an improved yield and a lower

fall-off of production rate with culture time is achieved. In an example, culture of *B. lactofermentum*, transformed by plasmid pCAB, at 31.5 deg produced 23.0 g/l L-lysine after 40 hr, and 45.0 g/l after 72 hr. (90pp)

L9 ANSWER 84 OF 113 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
ACCESSION NUMBER: 1991-08786 BIOTECHDS
TITLE: Control of the lysine biosynthesis sequence in *Corynebacterium glutamicum* as analyzed by overexpression of the individual corresponding genes; feedback inhibition resistant aspartate-kinase and dihydrodipicolinate-synthase gene cloning and expression
AUTHOR: Cremer J; Eggeling L; Sahm H
CORPORATE SOURCE: Kernforsch.Juelich
LOCATION: Institut fuer Biotechnologie 1 des Forschungszentrums Juelich GmbH, D-5170 Juelich, Germany.
SOURCE: Appl.Environ.Microbiol.; (1991) 57, 6, 1746-52
CODEN: AEMIDF
DOCUMENT TYPE: Journal
LANGUAGE: English
AN 1991-08786 BIOTECHDS
AB A gene cluster encoding feedback inhibition resistant aspartate-kinase (EC-2.7.2.4, lysC-alpha and lysC-beta) and aspartate-semialdehyde-dehydrogenase (EC-1.2.1.11, asd) was cloned from the mutant *Corynebacterium glutamicum* MH20-22B. A fragment was isolated for separate expression of the kinase without asd production in wild-type *C. glutamicum* ATCC 1302, and was compared with other clones over-expressing each of the 6 genes converting aspartic acid to lysine. Over-expression of the kinase was sufficient alone to achieve lysine formation (38 mM). Also, over-expression of dihydrodipicolinate-synthase (EC-4.2.1.52) resulted in lysine formation, but in a lower amount (11 mM). The other 4 enzymes (asd, dihydrodipicolinate-reductase (EC-1.3.1.26), diaminopimelate-dehydrogenase (EC-1.4.1.16) and diaminopimelate-decarboxylase (EC-4.1.1.20)) had no effect on lysine secretion. When both relevant enzymes were expressed together from plasmid pJC50, a further increase in lysine yield was obtained. This information may be useful in lysine production strain improvement. (38 ref)

L9 ANSWER 87 OF 113 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
ACCESSION NUMBER: 1989-02067 BIOTECHDS
TITLE: Cloning and sequencing of the meso-diaminopimelate-D-dehydrogenase (ddh) gene of *Corynebacterium glutamicum*; involved in lysine biosynthesis
AUTHOR: Ishino S; Mizukami T; Yamaguchi K; Katsumata R; Araki K
LOCATION: Tokyo Research Laboratories, Kyowa Hakko Kogyo Co., Ltd., Machida-shi, Tokyo 194, Japan.
SOURCE: Agric.Biol.Chem.; (1988) 52, 11, 2903-09
CODEN: ABCHA6
DOCUMENT TYPE: Journal
LANGUAGE: English
AN 1989-02067 BIOTECHDS
AB The ddh gene of *Corynebacterium glutamicum* KY10755 encoding meso-diaminopimelate- (meso-DAP)-D-dehydrogenase (DDH, EC-1.4.1.16) involved in lysine biosynthesis was cloned in a DAP auxotroph (dapD4) of *Escherichia coli* TM132 by complementation of the DAP auxotroph. Localization of the gene by deletion analysis revealed that a 1.7 kb XhoI-KpnI fragment contained the ddh gene. The specific activity of DDH was increased 14-fold when *C. glutamicum* RRL-5 was transformed with a recombinant plasmid pCD2 harboring the ddh gene, probably due to the gene dosage effect. The ddh gene was sequenced, and the initiation codon for the open reading

frame was determined to be the ATG at 783. The coding region consisted of 960 nucleotides, corresponding to a protein of 320 amino acid residues. The NH₂-terminal residue of the purified DDH was threonine, suggesting that the first methionine residue is removed after the initiation of translation. Upstream from the coding region a potential Shine-Delgarno sequence was observed, preceded by promoter-like sequences. The introduction of the gene into some lysine-producing mutants is in progress. (31 ref)

L9 ANSWER 102 OF 113 LIFESCI COPYRIGHT 2006 CSA on STN
ACCESSION NUMBER: 88:95908 LIFESCI
TITLE: Regulation of enzymes of lysine biosynthesis in *Corynebacterium glutamicum*.
AUTHOR: Cremer, J.; Treptow, C.; Eggeling, L.; Sahm, H.
CORPORATE SOURCE: Inst. Biotechnol., Kernforschungsanlage Juelich GmbH, PF 1913, D-5170, FRG
SOURCE: J. GEN. MICROBIOL., (1988) vol. 134, no. 12, pp. 3221-3229.
DOCUMENT TYPE: Journal
FILE SEGMENT: J
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The regulation of the six enzymes responsible for the conversion of aspartate to lysine, together with homoserine dehydrogenase, was studied in *Corynebacterium glutamicum*. In addition to aspartate kinase activity, the synthesis of diaminopimelate decarboxylase was also found to be regulated. The specific activity of this enzyme was reduced to one-third in extracts of cells grown in the presence of lysine. Homoserine dehydrogenase was repressed by methionine (to 15% of its original activity) and inhibited by threonine (4% remaining activity). The twofold increase in homoserine dehydrogenase activity resulted in a decrease in lysine formation accompanied by the formation of isoleucine. In contrast, repression of homoserine dehydrogenase resulted in increased lysine formation. A similar increase of the flow of aspartate semialdehyde to lysine was found in strains with increased dihydronicotinate synthase activity, constructed by introducing the dapA gene of *Escherichia coli* (coding for the synthase) into *C. glutamicum*.

L9 ANSWER 105 OF 113 Elsevier BIOBASE COPYRIGHT 2006 Elsevier Science B.V. on STN
ACCESSION NUMBER: 2000242037 ESBIOBASE
TITLE: Pathway analysis and metabolic engineering in *Corynebacterium glutamicum*
AUTHOR: Sahm H.; Eggeling L.; de Graaf A.A.
CORPORATE SOURCE: H. Sahm, Institut fur Biotechnologie 1, Forschungszentrum Julich GmbH, D-52425 Julich, Germany.
SOURCE: Biological Chemistry, (2000), 381/9-10 (899-910), 64 reference(s)
CODEN: BICHF3 ISSN: 1431-6730
DOCUMENT TYPE: Journal; General Review
COUNTRY: Germany, Federal Republic of
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The Gram-positive bacterium *Corynebacterium glutamicum* is used for the industrial production of amino acids, e.g. of L-glutamate and L-lysine. During the last 15 years, genetic engineering and amplification of genes have become fascinating methods for studying metabolic pathways in greater detail and for the construction of strains with the desired genotypes. In order to obtain a better understanding of the central metabolism and to quantify the in vivo fluxes in *C. glutamicum*, the [¹⁴C]-labelling technique was combined with metabolite balancing to achieve a unifying comprehensive pathway analysis.

These methods can determine the flux distribution at the branch point between glycolysis and the pentose phosphate pathway. The *in vivo* fluxes in the oxidative part of the pentose phosphate pathway calculated on the basis of intracellular metabolite concentrations and the kinetic constants of the purified glucose-6-phosphate and 6-phosphogluconate dehydrogenases determined *in vitro* were in full accordance with the fluxes measured by the [^{1,3}C]-labelling technique. These data indicate that the oxidative pentose phosphate pathway in *C. glutamicum* is mainly regulated by the ratio of NADPH/NADP concentrations and the specific activity of glucose-6-phosphate dehydrogenase. The carbon flux via the oxidative pentose phosphate pathway correlated with the NADPH demand for L-lysine synthesis. Although it has generally been accepted that phosphoenolpyruvate carboxylase fulfills a main anaplerotic function in *C. glutamicum*, we recently detected that a biotin-dependent pyruvate carboxylase exists as a further anaplerotic enzyme in this bacterium. In addition to the activities of these two carboxylases three enzymes catalysing the decarboxylation of the C₄ metabolites oxaloacetate or malate are also present in this bacterium. The individual flux rates at this complex anaplerotic node were investigated by using [^{1,3}C]-labelled substrates. The results indicate that both carboxylation and decarboxylation occur simultaneously in *C. glutamicum* so that a high cyclic flux of oxaloacetate via phosphoenolpyruvate to pyruvate was found. Furthermore, we detected that in *C. glutamicum* two biosynthetic pathways exist for the synthesis of DL-diaminopimelate and L-lysine.

As shown by NMR spectroscopy the relative use of both pathways *in vivo* is dependent on the ammonium concentration in the culture medium. Mutants defective in one pathway are still able to synthesise enough L-lysine for growth, but the L-lysine yields with overproducers were reduced. The luxury of having these two pathways gives *C. glutamicum* an increased flexibility in response to changing environmental conditions and is also related to the essential need for DL-diaminopimelate as a building block for the synthesis of the murein sacculus.

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ACCESSION NUMBER: 1998275992 ESBIOBASE
TITLE: Site-specific inactivation of meso-Diaminopimelate-dehydrogenase gene(ddh) in a lysine-producing *Brevibacterium lactofermentum*
AUTHOR: Kim O.-M.; Park S.-H.; Lee K.-R.
CORPORATE SOURCE: K.-R. Lee, Department of Food and Nutrition, Yeungnam University, Gyeongsan 712-749, South Korea.
E-mail: Krlee@ynucc.yeungnam.ac.kr
SOURCE: Korean Journal of Applied Microbiology and Biotechnology, (1998), 26/5 (387-392), 26 reference(s)
CODEN: SMHAEH ISSN: 0257-2389

DOCUMENT TYPE: Journal; Article

COUNTRY: Korea, Republic of

LANGUAGE: Korean

SUMMARY LANGUAGE: English; Korean

AB *Brevibacterium lactofermentum*, a gram-positive bacteria, has both the diaminopimelate (DAP) pathway and meso-DAP-dehydrogenase (DDH) pathway for L-lysine biosynthesis. To investigate importance of DDH pathway and the related ddh gene in lysine production, we introduced site-specific mutagenesis technique. A 300 bp DNA fragment central to the meso-DAP-dehydrogenase gene (ddh) of *B. lactofermentum* was used to inactive chromosomal ddh gene via homologous recombination. Southern hybridization analysis confirmed that the chromosomal ddh gene was disrupted by the vector sequence. The *B. lactofermentum* ddh mutant obtained have an inactive DDH pathway. The results reveal that inactivation of the ddh gene in *B.*

lactofermentum leads to dramatic reduction of lysine production as well as decrease of the growth rate, indicating that the DDH pathway is essential for high-level lysine production as well as biosynthesis of meso-DAP.

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ACCESSION NUMBER: 1994125471 ESBIOBASE
TITLE: Synthesis and testing of heterocyclic analogues of diaminopimelic acid (DAP) as inhibitors of DAP dehydrogenase and DAP epimerase
AUTHOR: Abbott S.D.; Lane-Bell P.; Sidhu K.P.S.; Vederas J.C.
CORPORATE SOURCE: J.C. Vederas, Department of Chemistry, University of Alberta, Edmonton, Alta. T6G 2G2, Canada.
SOURCE: Journal of the American Chemical Society, (1994), 116/15 (6513-6520)
CODEN: JACSAT ISSN: 0002-7863
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Substrate analogues were synthesized and examined as inhibitors of diaminopimelic acid (DAP) dehydrogenase from *Bacillus sphaericus* and of DAP epimerase from *Escherichia coli*. These enzymes produce meso-DAP (3) (a precursor for L-lysine and for peptidoglycan) from L-tetrahydrodipicolinic acid (1) and LL-DAP (2), respectively. The epimerase was purified by an improved procedure and confirmed to require both carboxyl and both amino groups for substrate recognition using deuterium-exchange experiments with DAP isomers, L-lysine, D-lysine, L- α -aminopimelate, and racemic α -aminopimelate. An imidazole analogue of DAP (2S)-2-amino-3-(4-carboxyimidazol-1-yl)propanoic acid (4), was synthesized by condensation of benzyl imidazole-4-carboxylate (8) with N-benzyloxycarbonyl(Cbz)-L-serine β -lactone (9) (product structure confirmed by X-ray analysis) followed by hydrogenolytic deprotection. Two other analogues, (2S,5'R)-2-amino-3-(3-carboxy-2-isoxazolin-5-yl)propanoic acid (5) and its 5'S diastereomer 6, were prepared by condensation of methyl N-Cbz-L-allylglycinate (13) with methyl chlorooximidoacetate (14) followed by separation of isomers and deprotection with NaOH and Me.sub.3SiCl/NaI. Similar condensation of ethyl chlorooximidoacetate with ethylene and of 14 with ethyl acrylate generated isoxazolines, which were saponified to 2-isoxazoline-3-carboxylic acid (25) and 2-isoxazoline-3,5-dicarboxylic acid (26), respectively. None of the compounds show significant inhibition of DAP epimerase or DAP dehydrogenase with the exception of 6, which is a potent and specific inhibitor of DAP dehydrogenase. At pH 7.5 or 7.8, compound 6 shows competitive inhibition ($K(i) = 4.2 \mu M$) with tetrahydrodipicolinic acid (1) for the forward reaction and noncompetitive inhibition ($K(i) = 23 \mu M$) with meso-DAP (3) for the reverse process. Preliminary tests for antimicrobial activity demonstrate that 6 inhibits the growth of *B. sphaericus*, which relies exclusively on DAP dehydrogenase to produce 3.

L9 ANSWER 108 OF 113 BIOTECHNO COPYRIGHT 2006 Elsevier Science B.V. on STN
ACCESSION NUMBER: 1993:24153275 BIOTECHNO

TITLE: Molecular aspects of lysine, threonine, and isoleucine biosynthesis in *Corynebacterium glutamicum*
AUTHOR: Eikmanns B.J.; Eggeling L.; Sahm H.
CORPORATE SOURCE: Institut fur Biotechnologie, Forschungszentrum Julich GmbH, D-52425 Julich, Germany.
SOURCE: Antonie van Leeuwenhoek, International Journal of General and Molecular Microbiology, (1993-1994), 64/2 (145-163)

DOCUMENT TYPE: CODEN: ALJMAO ISSN: 0003-6072
 COUNTRY: Journal; General Review
 LANGUAGE: Netherlands
 SUMMARY LANGUAGE: English
 AN 1993:24153275 BIOTECHNO
 AB The Gram-positive bacterium *Corynebacterium glutamicum* is used for the industrial production of amino acids, e.g. of L-glutamate and L-lysine. In the last ten years genetic engineering methods were developed for *C. glutamicum* and consequently, recombinant DNA technology was employed to study the biosynthetic pathways and to improve the amino acid productivity by manipulation of enzymatic, transport and regulatory functions of this bacterium. The present review summarizes the current knowledge on the synthesis and overproduction of the aspartate derived amino acids L-lysine, L-threonine and L-isoleucine in *C. glutamicum*. A special feature of *C. glutamicum* is its ability to convert the lysine intermediate piperideine-2,6-dicarboxylate to diaminopimelate by two different routes, i.e. by reactions involving succinylated intermediates or by the single reaction of diaminopimelate dehydrogenase. The flux distribution over the two pathways is regulated by the ammonium availability. The overall carbon flux from aspartate to lysine, however, is governed by feedback-control of the aspartate kinase and by the level of dihydronicotinate synthase. Consequently, expression of *lysC*(FBR) encoding a deregulated aspartate kinase and/or the overexpression of *dapA* encoding dihydronicotinate synthase led to overproduction of lysine. As a further specific feature *C. glutamicum* possesses a specific lysine export carrier which shows high activity in lysine overproducing mutants. Threonine biosynthesis is in addition to control by the aspartate kinase tightly regulated at the level of homoserine dehydrogenase which is subject to feedback-inhibition and to repression. *C. glutamicum* strains possessing a deregulated aspartate kinase and a deregulated homoserine dehydrogenase produce lysine and threonine. Amplification of deregulated homoserine dehydrogenase in such strains led to an almost complete redirection of the carbon flux to threonine. For a further flux from threonine to isoleucine the allosteric control of threonine dehydratase and of the acetohydroxy acid synthase are important. The expression of the genes encoding the latter enzyme is additionally regulated at the transcriptional level. By addition of 2-oxobutyrate as precursor and by bypassing the expression control of the acetohydroxy acid synthase genes high isoleucine overproduction can be obtained.

L9 ANSWER 110 OF 113 CAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 1997:803726 CAPLUS
 DOCUMENT NUMBER: 128:60792
 TITLE: Production of L-lysine in genetically engineered coryneform bacteria
 INVENTOR(S): Hirano, Seiko; Sugimoto, Masakazu; Nakano, Eiichi; Izui, Masako; Hayakawa, Atsushi; Yoshihara, Yasuhiko; Nakamatsu, Tsuyoshi
 PATENT ASSIGNEE(S): Ajinomoto Co., Inc., Japan
 SOURCE: Eur. Pat. Appl., 63 pp.
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------|------|----------|-----------------|----------|
| EP 811682 | A2 | 19971210 | EP 1997-108764 | 19970602 |
| EP 811682 | A3 | 19980610 | | |

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| EP 811682 | B1 | 20040121 | | |
| R: DE, DK, ES, FR, GB, IT, NL | | | | |
| JP 09322774 | A2 | 19971216 | JP 1996-142812 | 19960605 |
| US 6090597 | A | 20000718 | US 1997-852730 | 19970507 |
| ES 2214567 | T3 | 20040916 | ES 1997-108764 | 19970602 |
| PL 186081 | B1 | 20031031 | PL 1997-320324 | 19970603 |
| CN 1171442 | A | 19980128 | CN 1997-112960 | 19970605 |
| BR 9703475 | A | 19980929 | BR 1997-3475 | 19970605 |
| PRIORITY APPLN INFO : | | | JP 1996-142812 | A 19960605 |

PRIORITY APPN. INFO.: AB

AB L-Lysine productivity and production rate are improved by sustaining in corynebacteria the aspartokinase (gene lysC) wherein feedback inhibition by L-lysine and L-threonine has been substantially remitted and successively potentiating a DNA encoding dihydrodipicolinate reductase (gene dapB), a DNA encoding dihydrodipicolinate synthetase (gene dapA), a DNA encoding diaminopimelate decarboxylase (gene lysA), and a DNA encoding diaminopimelate dehydrogenase (gene ddh). Plasmid pCABDL carrying the mutant gene lysC and genes dapA, dapB, ddh, and lysA was prepared and introduced into Brevibacterium lactofermentum strain AJ11082. The transformants were able to grow well and produce lysine 26.5 g/L after 40-h culture, as compared to 22.0 of that of the parental strain.

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